FOREWORD INTRODUCTION

TUNGSTEN CARBIDE

CAS N°: 12070-12-1

SIDS Initial Assessment Report

For

SIAM 21

Washington, DC, 18-20 October 2005

1.	**Chemical Name:**	**Tungsten Carbide**
2.	**CAS Number:**	**12070-12-1**
3.	**Sponsor Country:**	Germany Contact Point: BMU (Bundesministerium fuer Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D- 53048 Bonn
4.	**Shared Partnership with:**	-
5.	**Roles/Responsibilities of the Partners:**	-
•	Name of industry sponsor /consortium	H. C. Starck GmbH, D-38642 Goslar Bayer AG, Germany, D-51368 Leverkusen Contact person: Dr. Burkhardt Stock D-51368 Leverkusen Building 9115
•	Process used	The BUA Peer Review Process: see next page
6.	**Sponsorship History**	
•	How was the chemical or category brought into the SIDS Program?	by ICCA-Initiative
7.	**Review Process Prior to the SIAM:**	last literature search (update): 31 Mai 2005 (Human Health): databases medline, toxline; search profile CAS-No. and special search terms 9 May 2005 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search terms OECD/ICCA
8.	**Quality check process:**	IUCLID was used as a basis for the SIDS dossier. All data were checked and validated by BUA. A final evaluation of the human health part has been performed by the Federal Institute for Risk Assessment (BfR) and of the ecotoxicological part by the Federal Environment Agency (UBA).
9.	**Date of Submission:**	Deadline for circulation: July 22, 2005
10.	**Date of last Update:**	Last literature search: IUCLID Chapter 1: 2005-03-01, Chapters 2-4: 2003-10-01, Chapter 5: 2005-01-01

11. Comments:

OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
- Review o f validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
- In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number:	**12070-12-1**
IUPAC Name:	**Tungsten carbide**
Molecular Formula:	WC
Structural Formula:	WC
Molecular Weight:	195.85 g/mol
Synonyms:	Tungsten monocarbide
	α-tungsten carbide

Several phases of the binary system W-C have been described in literature (Gmelin, 1993). Of major importance is α-tungsten carbide (WC) which forms homogeneously only when tungsten and carbon are present in a nearly exact stoichiometric ratio of 49.5-50.5 mol % C (Tulhoff, 2000).

1.2 Purity/Impurities/Additives

For tungsten carbide of the grade HC the following elemental composition is reported (% w/w) (H. C. Starck, 2003):

Tungsten	> 93
Carbon	6.1
Iron	< 0.03

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties of **tungsten carbide**

Property	Value	Reference	IUCLID
Substance type	Inorganic compound	H. C. Starck, 2003	1.1.1
Physical state	Grey metallic powder	H. C. Starck, 2003	1.1.1
Melting point	2776 °C	Tulhoff, 2000	2.1
Boiling point at 1013 hPa	6000 °C	Lide, 1991	2.2
Density	15.63 g/cm^3 at 18 °C	Lide, 1991	2.3
Vapor pressure	Not determinable*	H. C. Starck, 2004	2.4
Partition coefficient n-octanol/water (log K_{ow})	Not calculable	Bayer Industry Services, 2005	2.5
Water solubility	< 0.1 mg/l at 20 °C	Cassella Aktiengesellschaft, 1995	2.6.1
Flash point	Non-inflammable	H. C. Starck, 2005	2.7
Auto flammability (ignition temperature)	Inflammable at > 300°C	H. C. Starck, 2005	2.8

*Based on the boiling point, the vapor pressure is expected to be extremely low

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Tungsten carbide is manufactured by direct carburization of tungsten with carbon (Roempp, 2003). Mixtures of metal and carbon black or graphite are heated at a temperature of 1400 - 2000 °C in vacuum or under hydrogen (Tulhoff, 2000):

$W + C \rightarrow WC$.

When heating a mixture of tungsten and carbon in a carbon tube or high-frequency furnace to ca. 2800 °C, cast tungsten carbide is obtained (Gmelin, 1993). However, most tungsten carbide is sold as powders with distinct ranges of grain sizes (Tulhoff, 2000).

Purity and grain size determine the physical properties and the technical applicability of tungsten carbide. Since milling changes the chemical composition and the shape of the grains, coarse powders of tungsten carbide can not be milled to obtain fine-grained powders. Instead, to obtain the desired industrial product, the particle size of the raw materials is carefully selected. The grain size of the product is also influenced by manufacturing parameters like temperature, reaction time, presence of humidity and hydrogen. Typical production lines start from tungsten ore (W, Nb, Fe-oxides), tungsten scrap, scheelite ($CaWO_4$), tungstic acid (H_2WO_4), and ammonium paratungstate ($(NH_4)_{10}W_{12}O_{41}$ x 5 H_2O). Typical intermediates are yellow (WO_3), blue (approximately W_4O_{11}), and brown tungsten oxide (WO_2). There are several methods for the manufacturing of the technical tungsten carbide powders (Tulhoff, 2000): Tungstic acid powder is reduced to tungsten by hydrogen

at 750 °C. The metal particles are carburized at 1400 °C. This method is applied for fine powders with an average grain size of 1 µm.

$H_2WO_4 + 3\ H_2 \rightarrow W + 4\ H_2O$
$W + C \rightarrow WC.$

Ammonium paratungstate can be converted to the blue tungsten oxide at 700 °C in a nitrogen stream. Reduction at 800 °C and carburization at 1400 °C yields powders 2 - 5 µm grain size.

$(NH_4)_{10}W_{12}O_{41}\ x\ 5\ H_2O \rightarrow 3\ W_4O_{11} + 10\ NH_3 + 10\ H_2O$

Ammonium paratungstate can also be roasted in air to yield yellow tungsten oxide, which is reduced by wet hydrogen at 950 °C and carburized at 1600 °C to yield tungsten carbide with a particle size of 10-20 µm.

$(NH_4)_{10}W_{12}O_{41}\ x\ 5\ H_2O \rightarrow 12\ WO_3 + 10\ NH_3 + 10\ H_2O$

Tungsten oxides, tungstic acid, ammonium paratungstate, and scheelite can also be carburized directly:

$WO_3 + 4\ C \rightarrow WC + 3\ CO$
$H_2WO_4 + 4\ C \rightarrow WC + 3\ CO + H_2O$
$(NH_4)_{10}W_{12}O_{41}\ x\ 5\ H_2O + 48\ C \rightarrow 12\ WC + 10\ NH_3 + 10\ H_2O + 36\ CO$
$CaWO_4 + 4\ C \rightarrow WC + CaO + 3\ CO.$

Tungsten or tungsten oxide can also be carburized by gases like carbon monoxide or methane

$WO_2 + CH_4 \rightarrow WC + 2\ H_2O$

Very fine tungsten carbide can also be obtained by reaction of tungsten ore or scrap with chlorine, followed by gas phase reduction with hydrogen, and carburization:

$W + 3\ Cl_2 \rightarrow WCl_6$
$WCl_6 + 3\ H_2 \rightarrow W + 6\ HCl$
$W + C \rightarrow WC.$

The global production is estimated to be 15 000 - 20 000 tonnes/a (Tulhoff, 2000). In Germany, the only manufacturer of tungsten carbide has a manufacturing capacity of 1000 - 5000 tonnes/a (H. C. Starck, 2005).

Table 2 Estimated production volume of tungsten carbide in 2004 (H. C. Starck, 2005).

Region	Estimated production volume (tonnes/a)
Western Europe	13 000
Eastern Europe	1600
USA	5800
Japan	4500
China	13 000
Others	1170
Global	Approximately 39 000

Tungsten carbide is used exclusively in industrial applications (Tulhoff, 2000). The following applications are reported by the German manufacturer for its products (H. C. Starck, 2005):

- Cemented carbides (> 85 %)
- Coatings (5 %)
- Other alloys (< 10 %)

Cemented carbides are sintered products of one or more carbide powders – usually tungsten carbide as the main component – with a metallic binder (cement), preferably cobalt. Due to the extreme hardness of tungsten carbide and tungsten carbide based sinter alloys, about 90 % of the global manufacturing volume is used for the manufacture of tools. Tungsten carbide is applied to improve the wear resistance of moving parts in machines like rolls and balls, of bearings, and nozzles, cutting and drilling tools, and mining equipment. Tungsten carbide cemented with copper or silver is used for electrical contacts and in fuel cells. Since most cemented carbides contain tungsten carbide, which gives them their extreme hardness and their high specific gravity, these alloys are referred to as hard metals and are often also termed “tungsten carbide”. The global production of hard metals was approximately 20 000 tonnes in 1985 (Tulhoff, 2000).

While the spectrum of available tungsten carbide grain sizes ranged from 2.0 to 5.0 µm in the mid 1920’s, the grain sizes of tungsten carbide powders now used in hard metals range from 0.5 µm to 50 µm, or even 150 µm for some very special applications (International Tungsten Association, 2005). Grades within the nanoparticle range are available for specific uses (e.g. as catalysts); this is, however, a very small fraction of the current tungsten carbide production.

According to the Nordic Product Registers, tungsten carbide was used in 169 preparations in Denmark and Sweden with a total tonnage of ca. 3000 tonnes/a in 2002. No consumer preparation is listed. For Finland and Norway there are confidential listings. Tungsten carbide is used as a raw material for the manufacture of metals (SPIN, 2005). The use of tungsten carbide results in the inclusion into or onto a matrix (SPIN, 2005), which is in consistence with the information given by the manufacturer (H.C. Starck, 2005), and with published information. The Swedish Product Register (2005) lists 25 products, containing 20 - 80 % WC, with a tonnage of 853 tonnes/a, and 88 products, containing 80 - 100 % WC, with a tonnage of 3543 tonnes/a. The most frequent use is given as "raw material for production of metals". The Swiss Product Register (2005) lists 12 commercial products with 10 - 80 % WC for galvanic purposes, but no consumer products.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Environmental information from manufacturing and processing of tungsten carbide is available for the H. C. Starck plant in Germany (H. C. Starck, 2005).

The exhausts from manufacturing and processing are connected to exhaust filters. Thus, at H. C. Starck, during production virtually no tungsten carbide is emitted into the atmosphere. In 2003, according to the current Official Emission Declaration, virtually no tungsten carbide (< 25 kg/a) was emitted into the atmosphere (H. C. Starck, 2005).

The carburization of tungsten or other precursors is virtually free of liquid water (H. C. Starck, 2005).

The air emissions of the H. C. Starck production site are monitored by an Environmental Surveillance Group (H. C. Starck, 2005).

2.2.2 Photodegradation

The photodegradation of tungsten carbide cannot be calculated with the EPIWIN estimation program. The structure of the molecule is not accepted by the program. Moreover, due to the inorganic character of the substance calculations are not appropriate for the substance (Bayer Industry Services, 2005).

2.2.3 Stability in Water

Due to the physical-chemical properties (*cf*. Table 1) of tungsten carbide, it is expected that the substance exists as insoluble particles in water. The water solubility was experimentally determined according to the Directive 92/69/EEC, A.6 "water solubility", comparable to OECD TG 105 (Cassella Aktiengesellschaft, 1995). Since less than 0.0001 g/l tungsten carbide is soluble in water, the substance can be regarded as insoluble in water. Furthermore, the substance is also insoluble in water and dilute acids, but forms soluble salts in hot mixtures of HNO_3 and HF (Tulhoff, 2000).

2.2.4 Transport between Environmental Compartments

The distribution of tungsten carbide between the environmental compartments cannot be calculated with the EPIWIN estimation program, since the structure of the molecule is not accepted. Also the distribution of tungsten carbide according to Mackay Level I cannot be calculated (Bayer Industry Services, 2005; Noack, 1995 a, b, c).

It is assumed that the vapour pressure of the substance is to be extremely low and thus, any processes of volatilization are unlikely to occur (Bayer Industry Services, 2005).

In the ambient atmosphere, tungsten carbide will exist solely in the particulate phase and may be removed from the air by wet and dry deposition (Bayer Industry Services, 2005).

2.2.5 Biodegradation

Due to its inertness and its low solubility in water (*cf*. Table 1) of tungsten carbide, it is expected that the substance exists as insoluble particles in the environment. Tungsten carbide is thus not bioavailable for microorganisms for degradation and on the other hand not degradable due to the inorganic character of the substance. Therefore no biodegradation can be expected (Bayer Industry Services, 2005).

2.2.6 Bioaccumulation

Measured bioconcentration factors (BCF) for tungsten carbide are not available.

Estimation of a possible bioaccumulation potential of tungsten carbide is not practicable with the EPIWIN estimation program, since the structure of the substance is not accepted. It is expected that bioaccumulation of tungsten carbide is unlikely to occur (Bayer Industry Services, 2005).

2.2.7 Geoaccumulation

There are no data on the terrestrial fate of tungsten carbide available.

The possible geoaccumulation potential of tungsten carbide cannot be calculated with the EPIWIN estimation program, because the structure of the substance is not accepted. In addition, calculations are not appropriate for the substance due to the inorganic character of the substance (Bayer Industry Services, 2005).

Since tungsten carbide exists in a hexagonal crystalline form as an uncharged, solid substance no adsorption to suspended solids and sediment is expected (Tulhoff, 2000). The substance will be deposited on the ground (Noack, 1995 a, c).

The hardness of tungsten carbide is 9+ (Mohs) in the solid form (Lewis, 1993).

2.2.8 Environmental Monitoring

Occurrence

No data available.

Waste/soil/sediments

In soil of the rear of a hard metal (cemented tungsten carbide) tool grinding factory elevated levels of cobalt were detected (13 g/kg soil), which decreased to 0.1 - 1.8 g/kg soil in the close vicinity of this factory (20 m away), and to the background level of 0.01 - 0.02 g/kg soil in the neighborhood (≥ 30 m). Cobalt was closely associated with tungsten (carbon not determined), and backscatter electron micrographs indicated that some heavy metal was in the form of hard metal, consisting of tungsten carbide cemented with cobalt. Thus, cobalt contamination also points to tungsten carbide soil loads. The authors suggested that poor waste management in the factory caused the contamination of the close vicinity of this factory (Abraham and Hunt, 1995).

Water

No data available

Air/aerosols

No data available

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure to tungsten carbide is primarily via inhalation of dust particles during manufacture or use. In the worldwide carbide industry (including also other carbides) in the 1960ies, about 35 000 people were employed, about one third in the USA (Coates and Watson, 1971). According to the US National Occupational Exposure Survey of 1981 – 1983, the estimated numbers of employees in the U.S. potentially exposed to tungsten carbide by occupation was estimated to be 5422 (including 376 females) (NIOSH, 2005).

Workplaces

At the H. C. Starck manufacturing site, tungsten carbide is manufactured by several processes, which have in common that tungsten carbide is formed at elevated temperature. The Sponsor company processes small amounts of tungsten carbide for quality check, research and development (*cf* Chapter 2.2.1). Tungsten carbide is sold for processing to customers all over the world. Tungsten carbide is transported in bags and drums (H. C. Starck, 2005).

Precautionary measures at the workplace

In accordance with national regulations and the principles of Responsible Care and Sustainable Development, at the Sponsor company the exposure of workers is reduced to the lowest technically practicable level (H. C. Starck, 2005).

Surveys of the H. C. Starck workplaces are performed according to German Technical Guidances TRGS 402 and TRGS 901. This includes regular surveys in the working area for any possible exposure to hazardous substances and tungsten carbide under all relevant work scenarios, and encompasses appropriate control measures (H. C. Starck, 2005).

To protect workers from exposure to tungsten compounds, several precautionary and protective measures are taken. Sampling, for instance, is performed with specially designed systems and filling systems are equipped with special suction devices. Repair and maintenance work is only carried out on parts of the manufacturing or processing systems which have been emptied. Special written permits are required which include a detailed description of the protective measures depending on the work to be done (e.g. particle filter masks (classification P2-P3)) (H. C. Starck, 2005).

Down stream users of tungsten carbide are informed on the recommended safety measures through a material safety data sheet (H. C. Starck, 2005).

Potential exposure at the workplace and biological monitoring

The main use of tungsten carbide is in the manufacture of cemented carbide ("hard metal", see also Chapter 2.1). Cemented carbide is a material made by "cementing" tungsten carbide grains in a binder matrix of cobalt metal by liquid phase sintering. Small amounts of other metals, for instance, nickel, may also be added. During the hard metal manufacturing process various tungsten compounds and tungsten metal are used in the different workshops. The tungsten species have different degrees of bioavailability and combined exposures to other compounds and metals are common. Therefore, a correlation between external tungsten exposure and tungsten levels in biological materials cannot be expected.

In Germany, no maximum workplace concentration (MAK value) has been set for tungsten carbide (DFG, 2004). Available data on workplace exposures and biological monitoring from the hard metal industry are reported in the following:

Tungsten was detected in the lungs of 5 workers employed in the manufacture or grinding of cemented tungsten carbide ("hard metal"). Mass spectrometry of the lungs of three of them showed additionally the presence of cobalt and in one case also of titanium. In the lung of this person the content of tungsten, titanium and cobalt was 3.0, 2.0, and 0.1 µg/g wet lung weight, respectively. No workplace air concentrations were reported (Coates and Watson, 1971).

In a historical study, high levels of tungsten were found by Lichtenstein, Bartl and Pierce (1975) in the wet grinding area of a hard metal tool manufacturing facility without exhaust ventilation system. The concentration of tungsten carbide (measured as tungsten) in breathing zone air samples (n = 25) ranged from < 0.2 to 12.8 mg/m^3 with a mean of 5.16 mg/m^3. The employee time-weighted average shift exposures ranged from 0.72 to 8.06 mg/m^3 with a mean of 3.93 mg/m^3. The authors described several measures to diminish the airborne concentrations, including the use of local exhaust ventilation.

Biological samples of a worker, who had worked for 13 years as a grinder in a small hard metal enterprise, were taken at 4 years after cessation of exposure and analysed by neutron activation for several heavy metals (Rizzato et al., 1986). Higher than control levels of tungsten (and of other metals, e.g. tantalum, cobalt) were found in lung tissue, bronchoalveolar lavage fluid (BALF), blood, and urine (Table 3). Tungsten accounted for 7.5 % of the total particulate matter at the workplace, iron for 10 %, and cobalt for 8 % (no information available on the rest of the particulate matter) (Rizzato et al., 1986). In continuation of their study, Rizzato et al. (1994) examined 4 workers with symptoms of hard metal lung disease. These workers also contained elevated tungsten levels in several biological materials (lung tissue, BALF, blood, urine, pubic hair, sperm, and nails). On the other hand, some biotic tungsten levels matched control values and no correlation between severity of disease and metal contents could be drawn from the data (Rizzato et al., 1994). Unfortunately, no exposure concentrations were measured (Rizzato et al., 1986; Rizzato et al., 1994).

Table 3 Amounts and ratios of tungsten concentrations in biological material from one worker relative to controls (Rizzato et al., 1986).

Biological material	Worker (ng/g) (n = 1)*	Controls (ng/g) (n = 17)*	Ratio Worker/Controls
Lung tissue	107 000	1.5	71 330
BALF	60	1.5	40
Blood	1.35	0.4	3.4
Urine	12	0.7	17.1

*mean values of 4 determinations

The contents of tungsten carbide and cobalt were determined in metal dusts collected at several work places in a hard metal production factory for cobalt-cemented tungsten carbide. Cobalt tended to aggregate on tungsten carbide particles. Cobalt and tungsten carbide were present in dust from grinding area and other workplaces of the factory with almost all of the powder particles being of respirable size. In some workplace areas the ratio of tungsten carbide to cobalt equalled the ratio of the raw materials, indicating that the dust stemmed from the hard metal manufacturing activities. The highest tungsten carbide concentration was 0.017 mg/m^3 (Yamada et al., 1987).

Neutron activation techniques were used to analyse several elements in biological samples of 30 workers occupationally exposed to hard metal dust (Nicolaou et al., 1987). The tungsten, chromium and cobalt concentrations in urine, pubic hair, and toe nails of workers exposed to hard metal dust were higher than those of controls. On the other hand, the blood of exposed workers contained less tungsten than the blood of unexposed people (Table 4). The authors give no explanation for the unexpectedly high level of tungsten in blood of unexposed persons; however, only three individuals served as control group and only the mean blood level of this group is reported.

Table 4 Tungsten concentrations in biological samples of workers exposed to hard metal dust (Nicolaou et al., 1987).

Group	Urine*	Blood*	Pubic hair*	Toe nails*
Factory A (n = 10)	12	3	12 000	17 000
Factory B (n = 7)	44	2.2	3900	2035
Factory C (n = 13)	2	0.8	837	1200
Control (n = 3)	0.4	4.2	15	18

*ng W/g wet weight

In a comprehensive study on 251 workers with history of hard metal exposure, Sabbioni et al. (1994) examined tungsten concentrations in the workplace air and analysed tungsten levels in specimens of blood, urine, pubic hair, and toe nails collected from these workers. By neutron activation analysis, Sabbioni et al. (1994) found significant levels of tungsten and other metals (e.g. cobalt, data not shown) in the workplace air of hard metal factories in the Bergamo province (Table 5) and other areas of Northern Italy. Several biological specimens contained tungsten (Tables 6 and 7) and other heavy metals (data not shown).

Table 5 Tungsten concentration (mg/m^3) in airborne dust collected in the breathing zone of 4 factories in the Bergamo province (Sabbioni et al., 1994)

Factory/Operation	Fixed dust sampling Total dust	Fixed dust sampling < 7 µm	Personal monitoring
A/weighing	32	2.1	150
A/grinding	62	2.4	77
B/weighing	20	3.1	70
C/grinding	10.2	0.75	53
C/grinding	2.1	0.13	22
D/weighing	0.14	0.023	0.73

Table 6 Tungsten contents in biological specimens of hard metal workers of 4 factories in the Bergamo province (Sabbioni et al., 1994)

Specimens	n	Exposed workers Metal content (mean ± SD)	Unexposed subjects Metal content (mean*)
Blood	43	1.2 ± 1.6 µg/l	0.39 µg/l
Urine	78	6.7 ± 19.4 µg/l	0.32 µg/l
Pubic hair	75	2147 ± 5151 ng/g	12.4 ng/g
Toe nails	82	3056 ± 10 760 ng/g	18.0 ng/g

*) no standard deviations given by the authors

Table 7 Tungsten contents found in biological specimens of hard metal workers of the Milano area (Sabbioni et al., 1994)

Specimens	n	Exposed workers Metal content (mean ± SD)
Blood	16	1.29 ±2.7 µg/l
Urine	21	9.32 ± 6.5 µg/l
Pubic hair	20	7018 ± 16 570 ng/g
Toe nails	23	17 298 ± 32 470 ng/g
BALF	24	448 ± 602 µg/l*

*97.1 % in sediment, 2.9 % in supernatant

In the Pavia region air and urine samples were measured for 23 exposed workers involved in mixing powders for the preparation of diamond wheels. The tungsten concentrations (mean ± SD) were

- Airborne dusts: 0.026 ± 0.043 mg/m^3
- Urine: 2.29 ± 2.79 µg/l

In the Turin region biological samples were collected from 24 exposed workers. The tungsten contents (mean ± SD) were

- Urine: 12.8 ± 14.7 µg/l
- Pubic hair: 9585 ± 9159 ng/g

In the Milano area, a diseased hard metal worker was repeatedly examined after exposure to hard metal dust had ceased. The tungsten contents (as well as those of other metals) of the BALF of this worker decreased by half in the period between 6 and 18 months after exposure (Sabbioni et al., 1994):

- 6 months: 689 µg/l
- 8 months: 1350 µg/l
- 12 months: 700 µg/l
- 18 months: 340 µg/l.

Exposure to metallic tungsten, tungsten carbide, tungsten oxide, and tungstenate was assessed in a hard metal manufacturing factory involving 87 workers. Kraus et al. (2001) found tungsten at concentrations of up to 0.4 mg/m^3 in the air of these workplaces (Table 8). However, the measuring method did not distinguish between the species of tungsten e.g. metallic tungsten, tungsten carbide, tungsten oxide, and tungstenate.

Table 8 Ambient tungsten concentrations at different workplaces (Kraus et al., 2001)

Workplace	Sampling	n	Tungsten (µg/m³)
Forming	P	5	7.8 - 97
	S	1	6.2
Pressing	P	3	5.3 - 211
Powder processing	P	4	177 - 254
Production of tungsten carbide	P	1	19.1
Sintering	P	1	12.1
	S	1	5.9
Grinding (wet)	P	1	3.3
Grinding (dry)	P	1	81
Heavy alloy production	P	2	125 - 417
	S	3	50 - 163

P = personal sampling; S = stationary sampling.

33 subjects not occupationally exposed to tungsten were participating as controls. The urinary tungsten concentration (on a creatinine basis, Table 9) was not correlated to the concentration of tungsten in air. The 95 % percentile of the unexposed population was 1 µg/g creatinine. The highest tungsten concentration in urine (70.9 µg W/g creatinine) was found in a worker occupationally exposed to extremely low concentrations of tungstenate (3.3 µg W/m³, Table 10). Although the study is hampered by the low number of participants in the tungsten species exposure groups (Table 10), the authors concluded that the bioavailability of tungsten increases in the order: tungsten metal, tungsten carbide, tungstenate (Kraus et al., 2001). However; they did not take into account that traces of tungstenate might have contaminated other workplaces. It is noted, that the provided data actually indicate that tungsten carbide may be less bioavailable than tungsten metal.

Table 9 Urinary tungsten concentrations in workers from different workshops (Kraus et al., 2001)

Workshop	n	µg W/g creatinine (mean)
Forming	23	10.7
Pressing	30	8.6
Alloy production	3	24.9
Powder processing	14	12.2
WC production	4	42.1
Sintering	6	12.5
Grinding	5	94.4
Maintenance	2	3.4

Table 10 Ambient and biological monitoring of different tungsten species (Kraus et al., 2001)

Workshop	n	Tungsten species	Air (µg W/m³, mean and range)	Urine (µg W/g creatinine, mean and range)
Powder processing	4	W	203.5 (177 - 254)	13.8 (2.6 - 21.1)
Forming, pressing, sintering	8	WC	53.5 (5.3 - 211)	9.5 (2.2 - 33.1)
Grinding (dry)	1	WO_2, WC	81.3	10.6
WC production	1	WC, WO_2, W	19.1	59.6
Grinding (wet)	1	WO_4^{2-}	3.3	70.9

Goldoni et al. (2004) reported the exposure situation of workers in 3 factories involved in the production of either diamond tools or hard-metal inserts. All groups were exposed to tungsten carbide and cobalt concomitantly. The highest concentration of tungsten (most of it probably in the form of tungsten carbide) was 4.9 mg/m³ air, but most values were 1 - 3 orders of magnitude lower. The tungsten content in exhaled breath condensate (EBC) and in the urine of workers in 3 factories differed with the level of tungsten carbide (and cobalt) exposure (Table 11).

Table 11 Workplace tungsten concentrations and end-of-shift values [median (inter-quartile range)] of biomarkers in three factories **(Goldoni et al., 2004)**

Variables	n	Tungsten (mg/m³)	EBC (nmol W/l)	Urine (µmol W/mol creatinine)
Controls	16		< 0.5	< 0.06 (< 0.06 - 1.5)
Group A	10	< 0.01	< 0.5	< 0.06 (< 0.06 - 1.0)
Group B	11	0.10 (0.01 – 0.2)	1.1 (0.5 - 4.9)	1.2 (0.6 - 4.9)
Group C	12	3 (1.1 – 4.9)	25.6(15.2 - 76.1)	8.2 (3.2 - 16.1)

The median of the tungsten content in EBC of exposed workers ranged from < 0.5 to 25.6 nmoles/l. In urine the median tungsten content ranged between < 0.06 to 8.2 µmol/mol creatinine. In the EBC from controls, tungsten was not detectable. In exposed workers, EBC tungsten levels ranged from undetectable to 76 nmol/l. A parallel trend was observed for urinary tungsten concentrations. Tungsten levels were higher at the end of the work shift in comparison with preshift values (Goldoni et al., 2004).

2.3.2 Consumer Exposure

Consumer exposure to tungsten carbide is not likely to occur since all tungsten carbide is used in applications which result in the inclusion into or onto a matrix (SPIN, 2005) (*cf.* Chapter 2.1).

The information from the Nordic and Swiss Product Registers are consistent with the general use categories (*cf.* Chapter 2.1). It should be noted that these uses do not lead to consumer exposure.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

The absorption of tungsten carbide has been examined in an oral screening study in rats. Furthermore there is a single *in vitro* study on the solubility of tungsten carbide in human plasma and lung tissue cytosol. It is notable that passivating complexes may form with calcium ions on the surface of tungsten carbide particles, resulting in a drastic reduction of the solubility of tungsten carbide (Andersson and Bergström, 2000).

In addition, there are biomonitoring results available from workers occupationally exposed to hard metal dusts containing tungsten carbide.

Studies in Animals

In vivo Studies

2 female Sprague-Dawley rats (8 - 12 weeks old; 216 - 217 g bw) received a single dose of 2000 mg/kg bw tungsten carbide (suspended in 1 % methyl cellulose; 5 ml/kg bw) by oral gavage. One female rat served as control and received the vehicle only. Urine and feces were collected for 24 hours after dosing and then the animals were sacrificed. The tungsten contents in urine and feces as well as in shaved dorsal skin, gastrointestinal tract and carcass (without skin) were determined. The treatment was tolerated without clinical signs and at necropsy no pathological changes were observed. More than 98 % of the applied total tungsten was found in the feces, about 1 % in the gastrointestinal tract, and only 0.04 - 0.05 % was found in the urine (Bayer HealthCare AG, 2005).

Studies in Humans

In vitro Studies

The solubility of ^{187}W-tungsten after re-suspension of neutron-activated hard metal dust in human blood plasma and human lung tissue cytosol was very low (≤ 1 % of total [^{187}W]-radioactivity). After gel filtration the main part (> 90 %) of the radioactivity in plasma and cytosol was found to be associated with low molecular weight fractions (Edel et al., 1990).

In vivo Studies

In several studies on workers occupationally exposed to hard metal dust biomonitoring of tungsten has been performed. The highest concentration of tungsten was found in lung tissue; detectable amounts of tungsten were found in exhaled breath, bronchoalveolar lavage fluid, blood, urine, pubic hair, toe nails and in one case also in sperm (Rizzato et al., 1986; Nicolaou et al., 1987; Rizzato et al., 1994; Sabbioni et al., 1994; Kraus et al., 2001; Goldoni et al., 2004). For details: see chapter 2.3.1.

Conclusion

There is only limited information on the absorption, distribution and elimination of tungsten carbide available. Biomonitoring data of hardmetal workers (exposed to various tungsten compounds, including tungsten carbide) as well as *in vitro* studies with human blood plasma and lung tissue cytosol, respectively, indicate that the bioavailability of inhaled tungsten carbide is comparatively

low. Very low amounts of tungsten were found in the urine of 2 rats after single oral exposure to 2000 mg/kg bw of tungsten carbide.

3.1.2 Acute Toxicity

Valid studies are available to assess the acute inhalation, oral and dermal toxicity of tungsten carbide. Furthermore there are several valid non-guideline studies in rats and mice evaluating the effects of a single intratracheal instillation of tungsten carbide on the lung after different observation periods.

Studies in Animals

In vitro Studies

Tungsten carbide showed a low toxicity in freshly isolated rat alveolar epithelial type II cells and rat alveolar macrophages up to the highest concentration tested (1180 µg/100 000 cells) (Roesems et al., 1997).

In vivo Studies

Inhalation

In a study performed according to OECD TG 403 Sprague-Dawley rats were exposed snout-only for 4 hours to a tungsten carbide dust concentration of 5300 mg/m^3 supplied as particulate aerosol; MMAD was 7.3 µm; 48 % of the particles were of a respirable size (less than 7 µm in aerodynamic diameter). Control animals were exposed to clean air only. All animals survived without any clinical signs and any changes in body weight gain. There were no pathological findings at necropsy at study termination on day 14. The NOEL of this study is 5300 mg/m^3/4 hrs and the LC_{50} is greater than 5300 mg/m^3/4 hrs (Huntingdon Life Sciences Ltd., 1999a).

Dermal

In a study performed according to OECD TG 402 CD rats were treated with 2000 mg/kg bw tungsten carbide on the clipped and shaved dorsal skin for 24 hours under occlusion. No control group was included in this study; dermal absorption of the test substance was not determined. All animals survived without any clinical signs and any changes in body weight gain. There were no pathological findings at necropsy at study termination on day 15. The NOEL of this study is 2000 mg/kg bw and the LD_{50} is greater than 2000 mg/kg bw (Huntingdon Life Sciences Ltd., 1999b).

Oral

In two studies of different laboratories performed according to the former OECD TG 401(1981), CD rats and Sprague Dawley rats, respectively, were treated with 2000 mg/kg bw tungsten carbide by oral gavage. All animals survived without any clinical signs and any changes in body weight gain. There were no pathological findings at necropsy at study termination on day 15. In both studies the NOEL is 2000 mg/kg bw and the LD_{50} is greater than 2000 mg/kg bw (Laboratory of Pharmacology and Toxicology, 1994; Huntingdon Life Sciences Ltd., 1999c).

Other Routes of Exposure

8 female Sprague-Dawley rats were treated intratracheally with 10, 50 or 100 mg/kg bw tungsten carbide suspended in saline and sacrificed on day 1 or 28 after instillation. At both time points bronchoalveolar lavage (BAL) was done. Only a slight increase in number of total cells, macrophages and neutrophils in BAL fluid were observed on day 1 in the 50- and 100 mg/kg-

groups. Slightly increased levels of LDH, total protein and albumin were observed on day 1 at 100 mg/kg bw in the BAL fluid. On day 28, BAL showed no significant changes compared to the controls in any treatment group. The histopathological examination of the lungs yielded no indication of lung fibrosis (Lasfargues et al., 1995).

10 female Sprague-Dawley rats were instilled intratracheally with a tungsten carbide suspension of 157 mg/kg bw in physiological saline. 48 hours later animals were sacrificed and lungs were removed. In another experiment 5 females were treated with 10 mg/kg bw and 24 hours later bronchoalveolar lavage (BAL) was performed. Histopathological examination of lungs showed that 157 mg/kg bw tungsten carbide behaved as an inert dust producing only a mild accumulation of macrophages in the alveolar duct walls. Cellular and biochemical characteristics of bronchoalveolar lavage fluid at 10 mg/kg bw were not significantly different from those of control animals (Lasfargues et al., 1992).

3 female Sprague-Dawley rats were intratracheally instilled with saline suspensions of 10 mg/kg bw tungsten carbide. 24 hours later bronchoalveolar lavage was performed and evaluated. Examination of bronchoalveolar lavage fluid did not show any effect on production of inflammatory mediators and on lactate dehydrogenase activity, total protein or albumin content (Huaux et al., 1995).

Fifteen white rats were subjected to intratracheal instillation with 1 ml of a 10 % suspension of tungsten carbide (100 mg; ca. 400 mg/kg bw) in physiological saline. Rats were sacrificed at two-week-intervals for a total of 18 weeks. After 2 weeks the test substance was concentrated in the alveoli and septal walls. After 18 weeks wider dispersal of test substance was noted but no fibrogenic response was associated with the dust accumulations. No cellular reactions other than characteristic of an inert dust were observed (Miller et al., 1953).

2.5 mg of tungsten carbide were applied by intratracheal instillation (100 µl/animal in saline; ca. 100 mg/kg bw) to 80 NMRI mice. After 3, 15, 30 and 120 days respectively 20 animals each were sacrificed; 6 animals were used for bronchoalveolar lavage (BAL), 6 for preparation of lung homogenates, 4 for histopathology and 4 for mRNA analysis. Instillation of tungsten carbide did not induce significant changes in BAL fluid concerning LDH-level, protein content or number of cells. Histopathological examination after 120 days revealed an accumulation of particles in the lung parenchyma without any structural modification. The histological appearance of the lungs was similar to that of the vehicle-controls. The level of the interleukin 12-subunits p40 IL-12 and p70 IL-12 in BAL fluid remained unchanged whereas in lung tissue homogenate of tungsten carbide treated mice there was a transiently elevated p40 IL-12 level (significantly elevated on day 3; on day 15 back to control level). In BAL cell cultures the levels of p40 IL-12 and p70 IL-12 were also transiently elevated on day 3. In BAL cells the p40 IL-12-mRNA content was also elevated on day 3. The levels of IgG1 and IgG2 in BAL fluid remained unchanged. Overall tungsten carbide behaved like an innocuous dust in the lung (Huaux et al., 1999).

Female NMRI mice received a single intratracheal administration of 100 mg/kg bw tungsten carbide. Animals were sacrificed 1, 6 or 30 days post treatment and analyzed by bronchoalveolar lavage (BAL) analysis for total protein content, inflammatory cell number and -type and TNF-alpha production. The test substance induced a mild and transient inflammatory reaction which was observed only on day 1 after instillation. Tungsten carbide led to a small but not statistically significant elevation of the mean level of total protein in BAL fluid. However, tungsten carbide caused a prompt influx of polymorphonuclear leukocytes in the alveolar compartment but the total number of inflammatory cells remained unchanged compared to the control. No spontaneous release of TNF-alpha occurred at any time point in the absence of lipopolysaccharide (LPS). After LPS stimulation a strong reduction in TNF-alpha production on day 1 and a marked increase in TNF-alpha production on day 6 and 30 was observed (Broeckaert et al., 1997).

Tungsten carbide was administered intratracheally to groups of each 5 - 10 female NMRI mice (2 doses of 0.75 and 2.5 mg/mouse; total dose ca. 60 and 200 mg/kg bw, respectively). Bronchoalveolar lavage was done 1, 3, 5, 30, 60 and 120 days after application. Tungsten carbide showed no effects on plasminogen activator (urokinase), LDH-activity or total protein (Lardot et al., 1998).

In a study of which the reliability cannot be evaluated due to a lack of reported details, 10 male and 10 female rats were treated intratracheally with a single instillation of 30 mg tungsten carbide (ca. 120 mg/kg bw) suspended in 0.5 ml of distilled water with Tween 80. After 6 months the animals were sacrificed and examined. Histological examination of the sacrificed animals showed no treatment-related alterations. Tungsten carbide behaved like an inert dust (Schiller, 1958).

Studies in Humans

In vitro Studies

Tungsten carbide showed no toxicity in freshly isolated human alveolar epithelial type II cells up to the highest concentration tested (1180 µg/100 000 cells) (Roesems et al., 1997).

Conclusion

The acute toxicity of tungsten carbide is very low. The LC_{50} in rats is > 5300 mg/m^3/4 hrs and the LD_{50} after oral and the LD_{50} after dermal application is > 2000 mg/kg bw, respectively. No clinical signs were observed in any of these studies. Intratracheal instillation produces only moderate acute inflammation and minimal prolonged reactions. Under *in vitro* conditions tungsten carbide showed a low toxicity towards alveolar type II cells from rats, and no cytotoxicity towards human alveolar type II cells.

3.1.3 Irritation

There are valid studies available on skin and eye irritation which had been performed according to the OECD test-guidelines.

Skin Irritation

Studies in Animals

In a skin irritation test performed according to OECD TG 404 the dermal application of 0.5 mg tungsten carbide powder (moistened with 0.5 ml of distilled water) on the clipped back of three rabbits and subsequent 4 hour-exposure under semi-occlusive conditions did not lead to any signs of toxicity or ill health during the observation period of 72 hours. No dermal response to treatment was observed in any animal throughout the study (Huntingdon Life Sciences Ltd., 1999d).

Eye Irritation

Studies in Animals

In an eye irritation test performed according to OECD TG 405 with three days observation the instillation 100 mg of tungsten carbide powder into the eyes of three rabbits did not lead to corneal damage or iridial inflammation. A diffuse crimson coloration of conjunctiva with or without a slight swelling (grade 1 and 2) was seen in 2 rabbits up to 24 hours; in the remaining rabbit chemosis grade 1 was observed only 1 hour after instillation. At 48 hours after instillation all ocular reactions had resolved. Tungsten carbide showed only a transient very slight to well-defined conjunctival irritation (Huntingdon Life Sciences Ltd., 1999e). Based on the results of this study, tungsten carbide can be considered as non-irritant.

Respiratory Tract Irritation

In subchronic inhalation studies with rats and mice, which are presented in detail in chapter 3.1.5, there were indications for a mild irritating effect of tungsten carbide on the respiratory tract.of male rats and female mice exposed to 15 mg/m³ aerosolized tungsten carbide (MMAD 4.2 µm, geometric standard deviation 1.86) for 6 hours/day on 5 days/week for 13 weeks (Kutzman and Drew, 1986). At microscopic evaluation, the effects in rats were characterized by submucosal infiltration of mononuclear cells in the nasal cavity.

Conclusion

Tungsten carbide was not irritating to the skin and eyes of rabbits (OECD TG 404 and 405).

3.1.4 Sensitization

A valid skin sensitization assay on guinea pigs with tungsten carbide according to the OECD test guideline is available.

Studies in Animals

Skin

A guinea pig maximization test was performed according to OECD TG 406 (Huntingdon Life Sciences Ltd., 1999f). For induction 10 animals were treated by intradermal injection of 0.1 ml of a 50 % (w/v) suspension of tungsten carbide powder in Alembicol D (=fractionated coconut oil) with and without addition of Freund's complete adjuvant. After 6 days the skin area was clipped, shaved and pre-treated with sodium lauryl sulfate in petrolatum. 24 hours later a patch moistened with 0.4 ml of a 75 % (w/v) suspension of tungsten carbide in Alembicol D was applied to the same skin area and left for 48 hours under occlusive conditions for topical induction. Two weeks later the topical challenge was done by dermal application of 0.2 ml of a 75 % and 37.5 % tungsten carbide suspension in Alembicol D, respectively (exposure for 24 hrs under occlusion). The control group consisted of 5 animals which were treated likewise with the vehicle with and without Freund's complete adjuvant. After intradermal injection necroses were observed at all skin sites treated with Freund's complete adjuvans in test and control animals. Slight to well-defined irritation was seen in test animals at sites treated intradermally with 50 % suspension of tungsten carbide powder in Alembicol D and in control animals treated intradermally with Alembicol D. After topical induction slight erythema was observed in most test animals treated with 75 % tungsten carbide suspension in Alembicol D and slight erythema occurred in most of the control animals. After topical challenge there were no dermal reactions seen in any of the test or control animals; the black staining at the application site did not interfere with scoring. In this test tungsten carbide did not produce evidence of skin sensitization.

Conclusion

Tungsten carbide was not sensitizing in a guinea pig maximization test according to OECD TG 406.

3.1.5 Repeated Dose Toxicity

There are no studies available which had been performed to the OECD test-guideline but there are two valid subchronic inhalation studies on rats and mice available. Due to the fact that only one concentration was tested there is no NO(A)EL derivable. Furthermore there is a valid study with repeated intratracheal application available. Taken together, these studies provide sufficient information to address this endpoint.

Studies in Animals

Inhalation

Fischer-344 rats and B6C3F1 mice were whole-body exposed to 15 mg/m³ aerosolized tungsten carbide (MMAD 4.2 µm, geometric standard deviation 1.86) for 6 hours/day on 5 days/week for 13 weeks (Kutzman and Drew, 1986). In this well-conducted NTP-study, cobalt and tungsten carbide were investigated in parallel. Based on previous animal data, the test concentration for cobalt was set as 1 mg/m^3, and, because the ratio of cobalt to tungsten carbide in hard metal is usually 1 : 15, the tungsten carbide concentration was set at 15 mg/m^3. The control group was exposed to filtered air. The objective of the study was to relate a series of functional tests to compositional and structural alterations in the rat lung, induced by exposure to tungsten carbide. 24 male rats were designated for respiratory physiology studies (parameters of spontaneous breathing, electrocardiographic data, lung volumes, parenchymal behaviour, distribution of ventilation, flow volume dynamics). After pulmonary testing these animals were sacrificed and the left lung was processed for pathological examination while the right lung was submitted to biochemical analysis (weight, water content, protein, DNA, elastin, collagen). 8 rats/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs examined). After exposure to tungsten carbide, the pulmonary function tests showed no evidence of fibrogenic (restrictive) processes nor was there any indication of an obstructive lung disease. Similarly, hematological indices showed no effects. Protein and DNA content of lungs were slightly decreased when expressed in terms of dry lung weight. The alterations observed in the lungs of tungsten carbide exposed rats consisted of focal reactions around the end airways. These were characterized by minimal to moderate alveolar wall thickening with type II cell hyperplasia and accumulations of pigmented macrophages. Although chronic rhinitis was not detected in any of the female rats, the incidence in male rats appeared to be related to tungsten carbide exposure. This change was characterized by submucosal infiltration of mononuclear cells in the nasal cavity. Occasional lesions in non-respiratory tissues all appeared to be spontaneous.
The study with mice was run in parallel to the study with Fischer-344 rats. 8 mice/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs tested), but no functional tests of the lungs were conducted. Animals did not demonstrate marked lung alterations, although the females had chronic rhinitis. No other organ lesions in mice could be attributed to the treatment with tungsten carbide.

Overall, the impact of tungsten carbide exposures appears to have been marginal in this study, and it is debatable whether the effects constitute a significant pathological response. The LOEL for rats can be established at 15 mg/m³, based on mild histopathological alterations in the lungs (focal reactions around the end airways) and chronic rhinitis in males. The LOEL for mice was at 15 mg/m³, based on chronic rhinitis in females. The validity of the study is somewhat limited due to the fact that only one concentration has been tested; consequently no NOEL can be derived for rats and mice. Despite their limitations, these studies were well-conducted NTP-studies with adequate particle size distributions and detailed reporting, using an exposure level that exceeds the current US TLV for tungsten carbide, i.e. 5 mg/m^3 TWA and 10 mg/m^3 STEL.

In a study, of which the reliability cannot be assessed due to poor documentation, white rats were whole-body exposed for 1 hour daily over a period of 5 months to about 600 mg/m³ tungsten carbide dust. 77 % of the particles were smaller than 5 µm (Mezentseva, 1967; Kaplun and Mezencewa, 1960). The animals were sacrificed after the last exposure and examined. All animals remained healthy and gained body weight well. No macroscopic changes were detected. On microscopical examination no changes were found in any organ except for the lungs, where perivascular and peribronchial infiltration were observed. The walls of some of the small vessels were thickened, with loose fibers and a swollen endothelium. The interalveolar septa were thickened, due to the proliferation of lymphoid-histiocytic elements. Dust particles, mainly located

intracellularly, surrounded the vessels and were also found in the interalveolar septa. The LOEL in this study was 600 mg/m³ based on mild histopathological changes in the lung. The validity of this study is further limited as there was only one test concentration; consequently no NOEL can be derived.

Intratracheal Instillation

15 female Sprague-Dawley rats were instilled with 10 mg/kg bw tungsten carbide monthly over a period of 4 months. Evaluation of bronchoalveolar lavage fluid and histopathological examinations were done one month after the last treatment. No alterations of biochemical or cellular parameters or lung hydroxyproline content could be observed. Histopathology revealed no differences to sections of controls except for the presence of fine black particles deposited in alveolar macrophages (Lasfargues et al., 1995).

Oral

There were no studies with tungsten carbide available.

Studies in Humans

There are no studies with pure tungsten carbide available. Workers exposed to dust mixtures containing both cobalt and tungsten carbide ("hard metal dust"), are at risk of developing a variety of respiratory diseases (reviewed by Kelleher et al., 2000). These include reactive airways disease (occupational asthma) and the parenchymal diseases, such as giant cell interstitial pneumonitis, bronchiolitis obliterans, hypersensitivity pneumonitis, and interstitial fibrosis (hard metal disease, HMD). The pathogenesis of HMD is still unclear. An immunologic mechanism is suggested by the small percentage of workers affected and the known sensitizing capacity of cobalt. Alternatively, an interaction between cobalt and tungsten carbide has been suggested (Lison et al., 1995), in which tungsten carbide may act as an electron carrier to transfer electrons from cobalt to oxygen. Consequently, production of reactive oxygen species and free radicals may be responsible for pulmonary damage. The observation that few exposed workers develop interstitial disease may be explained by variability in individual antioxidant defenses. The necessity of an interaction between cobalt and other components in the pathogenesis of HMD, however, has recently been challenged by reports of interstitial lung disease in diamond polishers highly exposed to fine cobalt powder without tungsten carbide (cf. Kelleher et al., 2000).

Conclusion

Repeated inhalation of 15 mg/m³ tungsten carbide dust by rats caused chronic rhinitis and mild histopathological alterations in the lung consisting of focal reactions around the end airways. The changes were characterized by minimal to moderate alveolar wall thickening, type II cell hyperplasia and accumulations of pigmented macrophages. Mice exposed similarly to tungsten carbide tolerated the treatment without toxic symptoms except for rhinitis in females (LOEL, mice and rats, 13-weeks: 15 mg/m³ = lowest tested dose). Repeated intratracheal instillation of small doses of tungsten carbide to rats (10 mg/kg bw) yielded no alteration of bronchoalveolar lavage fluid composition and no histopathological changes in the lung except for the presence of fine black particles in alveolar macrophages.

3.1.6 Mutagenicity

A bacterial mutagenicity test and a chromosomal aberration test *in vitro* on human lymphocytes were available which were both performed according to the OECD test guidelines. Furthermore

there are several valid non-guideline tests on genotoxicity *in vitro* which are also taken into consideration for evaluation of this endpoint.

Studies in Animals

In vitro Studies

A bacterial mutagenicity test was performed on *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 as well as on *Escherichia coli* strain WP2uvrA/pKM101 (CM 891) according to the OECD TG 471. Neither in the first nor in the second test was a substantial increase in revertant colony numbers over control counts observed with any of the tester strains following exposure to tungsten carbide at any concentration up to the highest dose tested (5000 µg/plate) in either the presence or absence of rat liver S9 mix. The positive controls were functional (Huntingdon Life Sciences Ltd., 2001a).

In a chromosomal aberration test performed according to OECD TG 473 isolated human lymphocytes were incubated with 2.44 - 312.5 µg/ml tungsten carbide powder in either the presence or absence of rat liver S9 mix. Two separate tests were performed. Because of precipitation of the test substance at 312.5 µg/ml, this concentration was selected as the highest test dose. No cytotoxicity was found at this dose. There was no increase in the number of polyploid metaphase cells compared to the solvent control.

In the first test using 3 hours treatment followed by 17 hours recovery tungsten carbide was inactive in the absence of S9 mix. In the presence of S9 mix tungsten carbide caused a statistically significant increase in the proportion of metaphase figures with chromosomal aberrations at 78.13 and 156.25 µg/ml when compared to the solvent control. No reproducible values were observed between replicate cultures at 78.13 µg/ml. However, cultures exposed to tungsten carbide at dose levels of 78.13 µg/ml and above contained cells with a frequency of aberrations (excluding gaps) that exceeded the upper 99 % limit of the historical negative control range.

In the second test using 20 hours continuous treatment (without S9 mix) and 3 hours treatment followed by 17 hours recovery (with S9 mix) tungsten carbide was inactive in the absence of S9 mix. In the presence of S9 mix tungsten carbide caused no statistically significant increase in the proportion of metaphase figures with chromosomal aberrations when compared to the solvent control at any dose level. However, the statistical significance was decreased due to high solvent control values (mean = 3 % excluding gaps) and cultures exposed to tungsten carbide at the two highest concentrations contained cells with a frequency of aberrations (excluding gaps) that exceeded the upper 99 % limit of the historical negative control range. The positive controls were functional. In summary tungsten carbide showed in this test no clastogenic activity without S9 mix but an equivocal evidence of clastogenic activity *in vitro* in the presence of S9 mix (Huntingdon Life Sciences Ltd., 2001b). There is some suspicion that this weak clastogenic activity might represent an artifact since a plausible explanation for a possible role of S9 mix in the generation of reactive tungsten carbide reaction products is missing.

In three Alkaline Comet Assays isolated human lymphocytes were incubated with 10 - 100 µg/ml tungsten carbide for 15 min at 37 °C. In two assays exposure of human lymphocytes up to 100 µg/ml did neither induce cytotoxicity nor changes in tail length or tail moment compared to controls. Nevertheless treated cells presented a relatively higher DNA content in the tail at 75 and 100 µg/ml than control comets. This elevation was only slight and not dose-dependent (Anard et al., 1997; De Boeck et al., 2003). In the other publication, tungsten carbide induced slight but statistically significant increases in tail length and tail moment at all concentrations tested but without clear dose-dependency (Van Goethem, Lison and Kirsch-Volders, 1997). At present, the relevance of these findings cannot be judged, because these test systems have not been validated.

In an alkaline elution assay human lymphocytes, labelled with 1 µCi/ml of [methyl-^{3}H]-thymidine-triphosphate, were incubated for 10 and 20 minutes, respectively, with 25 - 250 µg/ml tungsten carbide at 37 °C. Treatment of cells up to 250 µg/ml did not induce more DNA breaks than observed in controls. There was no cytotoxicity observed at any concentration (Anard et al., 1997).

Two different *in vitro* micronucleus assays have been performed on isolated human lymphocytes. The cells were treated with 10 - 100 µg/ml tungsten carbide for 15 minutes at 37 °C and then further incubated for a total of 72 hours. After 44 hours cytochalasin B was added to block cytokinesis. As a measure for cell cycle delay and/or cytotoxicity the relative division index (RDI) was used. In the first test a statistically significant, but not dose-dependent increase in micronuclei was observed at 50, 75 and 100 µg/ml. A decrease of the percentage of cytokinesis-blocked cells was observed at the highest concentration of 100 µg/ml which can either be a sign of cytotoxicity or of cell cycle delay. The validity of the test is limited since no independent repeat test was performed (Van Goethem, Lison and Kirsch-Volders, 1997). In the second test with independent repeat tungsten carbide did not induce statistically significant elevations of the number of micronucleated cells (De Boeck et al., 2003).

In vivo Studies

There are no *in vivo* genotoxicity studies available with tungsten carbide.

Studies in Humans

There are no genotoxicity studies available with tungsten carbide in humans.

Conclusion

Tungsten carbide was not mutagenic in the Ames test with and without metabolic activation. It has shown no evidence of clastogenic activity in cultured human lymphocytes in the absence of metabolic activation. There was, however, equivocal evidence of clastogenic activity with metabolic activation. *In vivo* data were not available.

3.1.7 Carcinogenicity

Studies in Animals

There were no data available

Studies in Humans

Epidemiological surveys have been conducted in the hard metal manufacturing industry and showed a potential association between exposure to hard metal dusts containing both, cobalt and tungsten carbide, and lung cancer (Wild et al., 2000). No studies were available on tungsten carbide itself.

Conclusion

There are no data available on this endpoint for tungsten carbide.

3.1.8 Toxicity for Reproduction

There were no studies available which specifically examined the effects of tungsten carbide on fertility and development. Based on physico-chemical and available animal data, which all indicate a very low bioavailability of tungsten carbide, exposure of the reproductive organs and of the developing organism is considered to be negligible. In addition, the results from subchronic

inhalation studies with tungsten carbide in rats and mice were used for the assessment of effects on reproductive organs.

Studies in Animals

Effects on Fertility

Results from subchronic inhalation studies (histopathology and weights of reproductive organs) were used in the assessment of this endpoint (cf. chapter 3.1.5 for the description of study details).

13-week-exposure of rats and mice to 15 mg/m³ aerosolized tungsten carbide dust led to marginal lung effects in rats and to rhinitis in male rats and female mice. All other organs of rats and mice which had been examined by histopathology (including testes, epididymides, prostata, uterus and ovary) showed no treatment-related alterations. Testes weights were not different from the control values (Kutzman and Drew, 1986).

In a poorly documented study, of which the reliability cannot be assessed, rats were whole-body exposed for 1 hour daily over a period of 5 months to about 600 mg/m³ tungsten carbide dust. 77 % of the particles were smaller than 5 µm (Mezentseva, 1967; Kaplun and Mezencewa, 1960). The animals were sacrificed after the last exposure and examined. All animals remained healthy and gained body weight well. No macroscopic changes were detected. On microscopical examination no changes were found in any of the internal organs except in the lungs.

Based on the analysis of the available data (histopathology of reproductive organs, testis weights), there is no indication of a possible impairment of reproductive functions by inhaled tungsten carbide.

Developmental Toxicity

There are no studies available to assess the developmental toxicity of tungsten carbide. However, based on physico-chemical and limited animal data tungsten carbide has a very low bioavailability and has only minimal systemic effects, even if repeatedly administered to laboratory animals (Kutzman and Drew, 1986; Mezentseva, 1967; Kaplun and Mezencewa, 1960). There is, therefore, no indication that reproductive organs or the developing organism may be adversely affected by tungsten carbide.

Studies in Humans

There are no studies available with tungsten carbide in humans concerning the toxicity for reproduction.

Conclusion

There were no studies available which examined the effects of tungsten carbide on fertility and development. Based on the histopathological examinations of reproductive organs and testis weights insubchronic inhalation of tungsten carbide dust in rats and mice there is no indication of a possible impairment of fertility by inhalative exposure to tungsten carbide dust. There are no studies available to assess the developmental toxicity of tungsten carbide. However, tungsten carbide has a very low bioavailability and has only minimal systemic effects, even if repeatedly administered to laboratory animals. There is, therefore, no indication that reproductive organs or the developing organism may be adversely affected by tungsten carbide.

3.2 Initial Assessment for Human Health

There is only limited information on the absorption, distribution and elimination of tungsten carbide available. Biomonitoring data of hard metal workers (exposed to various tungsten compounds, including tungsten carbide) as well as *in vitro* studies with human blood plasma and lung tissue cytosol, respectively, indicate that the bioavailability of inhaled tungsten carbide is comparatively low. Very low amounts of tungsten were found in the urine of 2 rats after single oral exposure to 2000 mg/kg bw of tungsten carbide.

The acute toxicity of tungsten carbide is very low. The LC_{50} in rats is > 5300 mg/m^3/4 hrs and the LD_{50} after oral and the LD_{50} after dermal application is > 2000 mg/kg bw, respectively. No clinical signs were observed in any of these studies. Intratracheal instillation produces only moderate acute inflammation and minimal prolonged reactions. Under *in vitro* conditions tungsten carbide showed a low toxicity towards alveolar type II cells from rats, and no cytotoxicity towards human alveolar type II cells.

Tungsten carbide was not irritating to the skin and eyes of rabbits (OECD TG 404 and 405) and not sensitizing in a guinea pig maximization test according to OECD TG 406.

Repeated inhalation of 15 mg/m³ tungsten carbide dust by rats caused chronic rhinitis and mild histopathological alterations in the lung consisting of focal reactions around the end airways. The changes were characterized by minimal to moderate alveolar wall thickening, type II cell hyperplasia and accumulations of pigmented macrophages. Mice exposed similarly to tungsten carbide tolerated the treatment without toxic symptoms except for rhinitis in females (LOEL, mice and rats, 13-weeks: 15 mg/m³ = lowest tested dose). Repeated intratracheal instillation of small doses of tungsten carbide to rats (10 mg/kg bw) yielded no alteration of bronchoalveolar lavage fluid composition and no histopathological changes in the lung except for the presence of fine black particles in alveolar macrophages.

Tungsten carbide was not mutagenic in the Ames test with and without metabolic activation. It has shown no evidence of clastogenic activity in cultured human lymphocytes in the absence of metabolic activation. There was, however, equivocal evidence of clastogenic activity with metabolic activation. *In vivo* data were not available.

There was no data available concerning the carcinogenicity of tungsten carbide.

There were no studies available which examined the effects of tungsten carbide on fertility and development. Based on the histopathological examinations of reproductive organs and testis weights in subchronic inhalation studies of tungsten carbide dust in rats and mice there is no indication of a possible impairment of fertility by inhalative exposure to tungsten carbide dust. There are no studies available to assess the developmental toxicity of tungsten carbide. However, tungsten carbide has a very low bioavailability and has only minimal systemic effects, even if repeatedly administered to laboratory animals. There is, therefore, no indication that reproductive organs or the developing organism may be adversely affected by tungsten carbide.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Concerning the acute toxicity of tungsten carbide towards aquatic species, experimental data are available for three trophic levels (*cf.* Table 12). In all tests, a stock solution was prepared by weighing the amount of test substance into water. The stock solutions were treated in ultrasonic

baths and then were stirred for 24 h before preparing the dilutions. The test designed leads to the conclusion, that all test solution were saturated. All tests were conducted with nominal concentrations high above the water solubility of tungsten carbide.

The toxicity to fish (*Danio rerio*) was conducted in a static test according to the OECD TG 203 "Fish, Acute toxicity test" (Noack, 1995a). The substance was separately weighted for each test concentration, added to the test media, and dispersed by ultrasonic for 30 min. Sedimentation of the tungsten carbide was observed in all test vessels. The settled test substance was dispersed twice daily with an ultraturrax. The stability of the test substance was experimentally determined (photometrically at 640 nm after derivatization with 3,4-dimercaptotoluene) at test start and end. Recovery rates were > 77 % at test end. Effect level concentrations are given as nominal concentrations which were high above the water solubility of tungsten carbide. Since no effect was observed at the highest test concentration of 1000 mg/l, a 96 h-LC_{50} of > 1000 mg/l is derived.

A test on the acute toxicity of tungsten carbide to the invertebrate *Daphnia magna* was performed according to the OECD TG 202 (Noack, 1995b). A tungsten carbide suspension of 2000 mg/l prepared by shaking was used to obtain test suspensions by dilution (32-1000 mg/l). The stock solution was not filtered before preparing the test solutions. Due to the insolubility of tungsten carbide in dilution water, the test substance was deposited on the ground. During magnetic stirring for 3 min samples were taken for analysis at the start of the experiments before addition of daphnias, and at the end of the test. Although recoveries were 65- 82 %, the results were related to nominal concentrations because loss of the test substance occurred during the sampling procedure. Low recovery rates were attributed to the insolubility and sedimentation of tungsten carbide in the test medium during sampling. At the highest test concentration of 1000 mg/l no effects were observed at 24 hours and only a small effect (3/20 daphnias) after 48 hours. An EC_{50} of > 1000 mg/l is derived directly from the test results.

Concerning the algae toxicity, a guideline study with *Desmodesmus subspicatus* in the presence of tungsten carbide was performed according to the European Directive 92/69/EEC, C.3 "Algal inhibition test", comparable to OECD TG 201 (Bayer AG, 2000). Since tungsten carbide is hardly soluble in water, the analytical monitoring was omitted. The test was conducted as a limit test at a concentration of 1 mg/l which is high above the water solubility of tungsten carbide. Tungsten carbide was weighted and added directly to test media. It was treated with ultrasonic for 1 hour and subsequently stirred for another 24 hours. Undissolved tungsten carbide was removed by filtration before the algae were added. No effects were observed at the concentration tested. Thus, an EC_{50} of > 1 mg/l can be derived.

Chronic Toxicity Test Results

No tests on chronic toxicity are available.

Table 12 Toxicity of tungsten carbide to **aquatic species**

Species	Test type	Parameter	Effects	Reference	IUCLID
Danio rerio	static	96 h-LC_{50}	> 1000 mg/l (n)	Noack, 1995a	4.1
Daphnia magna	static	48 h-EC_{50}	> 1000 mg/l (n)	Noack, 1995b	4.2
Desmodesmus subspicatus	static	Growth rate and biomass 72 h-EC_{50}	> 1 mg/l (n)	Bayer AG, 2000	4.3

(n): nominal concentration

Based on these data, tungsten carbide is considered as not harmful to aquatic organism.

Toxicity to Microorganisms

Toxicity of tungsten carbide to activated sludge was evaluated by Noack (1995c) according to the OECD TG 209. The test substance was not soluble in water in a concentration of 1000 mg/l and deposited on the ground. Effects of the test concentration leading to an inhibition > 20 % after 3 hours were not observed. An EC_{50} of > 1000 mg/l is derived from the test results.

Table 13 Tests on toxicity of tungsten carbide to microorganisms (IUCLID 4.4)

Species	Endpoint	Parameter	Effects	Reference	IUCLID
Activated Sludge	Respiration inhibition	3 h-EC_{50}	> 1000 mg/l (n)	Noack, 1995c	4.4

n): nominal concentration

Based on these data, tungsten carbide is considered as not harmful to microorganism.

4.2 Terrestrial Effects

No data available.

4.3 Other Environmental Effects

No data available.

4.4 Initial Assessment for the Environment

Tungsten carbide is a grey metallic powder with a melting point of 2776 °C, and a boiling point of 6000 °C at 1013 hPa. The density is 15.63 g/cm³ at 18 °C. Based on the boiling point, the vapor pressure is expected to be extremely low. The solubility in water is < 0.0001 g/l at 20 °C. The substance is insoluble in water and dilute acids, but forms soluble salts in hot mixtures of HNO_3 and HF.

Photodegradation, the octanol-water coefficient, a possible bio- and geoaccumulation potential can not be calculated with the EPIWIN estimation program. Furthermore, also the distribution of tungsten carbide according to Mackay Level I cannot be estimated.

Due to the negligible vapor pressure of the substance, any processes of volatilization are unlikely to occur. In the ambient atmosphere, the substance will exist solely in the particulate phase and may be removed from the air by wet and dry deposition.

Due to the physical-chemical properties of tungsten carbide biodegradation and bioaccumulation of the substance are unlikely to occur.

Tungsten carbide exists in a hexagonal crystalline form as an uncharged solid substance and therefore no adsorption to suspended solids and sediment can be expected.

Concerning the toxicity of tungsten carbide to aquatic species reliable acute experimental results of tests with fish, *Daphnia*, and algae are available. The tests were performed according to standard procedures and were conducted with nominal concentrations high above the water solubility of tungsten carbide. The effect values from short-term tests are (n= nominal concentration):

Danio rerio:	96 h-LC_{50}	> 1000 mg/l (n)
Daphnia magna:	48 h-EC_{50}	> 1000 mg/l (n)
Desmodesmus subspicatus:	72 h-$EC_{50growth\ rate}$	> 1 mg/l (n)

Based on these data, tungsten carbide is not toxic to aquatic organism at its water solubility.

5 RECOMMENDATIONS

Human Health:

The chemical is a candidate for further work. The chemical possesses properties indicating a hazard (indications for a clastogenic activity *in vitro*). While exposure of consumers is anticipated to be negligible, exposure to tungsten carbide occurs in occupational settings. The equivocal results in clastogenicity tests *in vitro* should be further investigated for clarification of possible human relevance.

Environment:

The chemical is currently of low priority for further work because of its low hazard profile.

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I U C L I D

Data Set

Existing Chemical	:	ID: 12070-12-1
CAS No.	:	12070-12-1
EINECS Name	:	tungsten carbide
EC No.	:	235-123-0
TSCA Name	:	Tungsten carbide (WC)
Molecular Formula	:	CW

Producer related part

Company	:	H.C. Starck GmbH & Co. KG
Creation date	:	17.02.1994

Substance related part

Company	:	H.C. Starck GmbH & Co. KG
Creation date	:	17.02.1994
Status	:	
Memo	:	
Printing date	:	23.12.2005
Revision date	:	17.02.1994
Date of last update	:	23.12.2005
Number of pages	:	67
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name : Tungsten carbide
Smiles Code :
Molecular formula : WC
Molecular weight : 195.85 g/mol
Petrol class :

Remark : Molecular weight is calculated from
W = 183.84
C = 12.011
==> 195.85 g/mol
Flag : Critical study for SIDS endpoint
18.07.2005 (1) (2)

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : inorganic
Physical status : solid
Purity : >= 99.1 % w/w
Colour : grey
Odour : none

Flag : Critical study for SIDS endpoint
15.06.2005 (3) (4)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Tungsten monocarbide

Flag : Critical study for SIDS endpoint
08.03.2005 (5)

alpha-tungsten carbide

Flag : Critical study for SIDS endpoint

08.04.2005 (2)

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 7439-89-6
EC-No : 231-096-4
EINECS-Name : iron
Molecular formula : Fe
Value : < .03 % w/w

Flag : Critical study for SIDS endpoint
15.06.2005 (3)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : ca. 15000 - 20000 tonnes produced in

Remark : - The global production volume of tungsten carbide was approximately 15000-20000 tonnes in 1985
- The global production of hard metals was approximately 20000 tonnes in 1985

Flag : Critical study for SIDS endpoint
23.12.2005 (2)

1.6.1 LABELLING

Labelling : no labelling required (no dangerous properties)
Specific limits : no

03.05.2005 (6) (4)

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :

19.07.2005 (6) (4)

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use resulting in inclusion into or onto matrix

Flag : Critical study for SIDS endpoint
23.12.2005 (7)

Type of use : industrial
Category : other: Tungsten carbide is not listed to be used as a consumer product

Result : According to the Nordic Product Registers, tungsten carbide was used in 169 preparations in Denmark and Sweden with a total tonnage of ca. 3000 tonnes/a in 2002. No consumer preparation is listed. For Finland and Norway there are confidential listings
Flag : Critical study for SIDS endpoint
23.12.2005 (7)

Type of use : use
Category : other: Manufacture of fabricated metal products

Result : Tungsten carbide is used as a raw material for the manufacture of metals
Flag : Critical study for SIDS endpoint
23.12.2005 (7)

Type of use : type
Category : Use resulting in inclusion into or onto matrix

Result : While the spectrum of available tungsten carbide grain sizes ranged from 2.0 to 5.0 µm in the mid 1920's, the grain sizes of tungsten carbide powders now used in hard metals range from 0.5 µm to 50 µm, or even 150 µm for some very special applications. Grades within the nanoparticle range are available for specific uses (e.g. as catalysts); this is, however, a very small fraction of the current tungsten carbide production
Flag : Critical study for SIDS endpoint
23.12.2005 (8)

Type of use : industrial
Category : other: Raw material for production of metals

Result : The Swedish Product Register lists 25 products, containing 20 - 80 % WC, with a tonnage of 853 tonnes/a, and 88 products, containing 80 - 100 % WC, with a tonnage of 3543 tonnes/a. The most frequent use is given as "raw material for production of metals"
Flag : Critical study for SIDS endpoint
23.12.2005 (9)

Type of use : industrial
Category : Metal extraction, refining and processing of metals

Result : The Swiss Product Register lists 12 commercial products with 10 - 80 % WC for galvanic purposes, but no consumer products
Flag : Critical study for SIDS endpoint
23.12.2005 (10)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)
Limit value :

Remark : No maximum workplace concentration (MAK) value has been established for tungsten carbide
15.06.2005 (11)

Type of limit : TLV (US)
Limit value : 5 mg/m3

Flag : Critical study for SIDS endpoint
28.02.2005 (12)

Type of limit : other: German threshold limit value (TRGS 900)
Limit value : 5 mg/m3

Remark : Insoluble tungsten compounds; calculated as W; limit value with reference to the inhalable fraction
Flag : Critical study for SIDS endpoint
15.06.2005 (13)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : other: VwVwS
Labelled by : other: VwVwS
Class of danger :

Remark : Class of danger: nwg (nicht wassergefaehrdend; non-hazardous to water) Classification according to Annex 3 of the Administrative Regulation of Substances Hazardous to Water (VwVwS). Substance No.: 5860
03.05.2005 (14)

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Number : other: 5.2.1
Class of danger :

Remark : Total particulate matter. The particulate matter in the exhaust shall not exceed the limit value of 0.20 kg/h or the concentration of 20 mg/m3
11.03.2005 (15)

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

Memo : CAS No. 12070-12-1 replaces CAS Nos. 182169-08-0, 182169-11-5, 188300-42-7, 188300-43-8, 188300-44-9, 188300-45-0 and 52555-87-0

25.02.2005 (1)

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered : 5
Date of search : 01.01.2005

01.03.2005

Type of search : Internal and External
Chapters covered : 2
Date of search : 01.10.2003

02.03.2005

Type of search : Internal and External
Chapters covered : 3
Date of search : 01.10.2003

02.03.2005

Type of search : Internal and External
Chapters covered : 4
Date of search : 01.10.2003

02.03.2005

1.13 REVIEWS

2.1 MELTING POINT

Value : 2776 °C
Sublimation :
Method :
Year : 2000
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
Flag : Critical study for SIDS endpoint
15.06.2005 (2)

Decomposition : yes, at 2800 °C
Sublimation :
Method :
Year : 1999
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
15.03.2005 (16)

Decomposition : yes, at ca. 2785 °C
Sublimation :
Method :
Year : 1989
GLP : no data
Test substance : other TS: tungsten carbide, 6.1 % C according to phase diagram

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
15.06.2005 (17)

Value : ca. 2870 °C
Sublimation :
Method :
Year : 1991
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Result : +/- 50 °C
Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
13.03.2005 (18)

Value : 2780 °C
Sublimation :
Method :
Year : 1993
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
25.02.2005 (19)

Value : 2730 - 2830 °C
Sublimation :
Method :
Year : 2003
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
16.06.2005 (5)

Decomposition : yes, at 2500 - 2700 °C
Sublimation :
Method :
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Manufacturer data without proof
15.03.2005 (4)

2.2 BOILING POINT

Value : 6000 °C at 1013 hPa
Decomposition :
Method :
Year : 1991
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
Flag : Critical study for SIDS endpoint
17.03.2005 (18)

Value : 6000 °C at 1013 hPa
Decomposition :
Method :
Year : 1993
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
15.06.2005 (5) (19)

2.3 DENSITY

Type : density
Value : 15.63 g/cm³ at 18 °C
Method :
Year : 1991
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
Flag : Critical study for SIDS endpoint
15.03.2005 (18)

Type : density
Value : 15.7 g/cm³ at °C
Method :
Year : 1999
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
21.03.2005 (16) (2)

Type : density
Value : 15.6 g/cm³ at °C
Method :
Year : 1993
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
21.03.2005 (5) (19)

Type : density
Value : 15.7 g/cm³ at °C
Method :
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Remark : A bulk density between 2000-3000 kg/m³ is reported.
Reliability : (4) not assignable
Manufacturer data without proof
15.03.2005 (4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Decomposition :
Method :
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Remark : Not relevant. Based on the boiling point, the vapor pressure is expected to be extremely low
Reliability : (4) not assignable
Manufacturer data without proof
Flag : Critical study for SIDS endpoint
17.03.2005 (4)

2.5 PARTITION COEFFICIENT

Remark : Not calculable by EPIWIN KOWWIN V 1.67, 2000
Flag : Critical study for SIDS endpoint
21.03.2005 (20)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : < .1 mg/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: Directive 92/69/EEC, A.6, comparable to OECD TG 105
Year : 1995
GLP : yes
Test substance : other TS: tungsten carbide, purity > 99 %

Method : The column elution method was not suitable to determine the water solubility. It was not possible to fix tungsten carbide on the carrier material. Therefore the flask method to determine the water solubility was selected.
Remark : Because of the expected low water solubility the preliminary test was not carried out.
Result : Single measurements range between 0.03 and 0.09 mg/l (i. e. 30 to 90 ppb) with two blank values at 0.01 and 0.02 mg/l (i. e. 10 and 20 ppb)
Test condition : TEST SYSTEM:
- test vessel: 1000 ml glass bottle, thermostated in a cryostath (Lauda RMS 6), shaking from time to time for approx. 30 seconds
- temperature: 20. 0 °C
- pH: 7.5 - 8.1
- test concentration: 10 mg/l
- blank test: 100 ml reagent water
- sample treatment: filtration and pH-measurement, afterwards 0.2 ml of nitric acid was added to the sample
- analysis: ICP-OES-Spectrometer (Liberty 100, Varian), detection by measuring the light absorbancy at 207.911 nm; every solution injected three times

Test substance : Batch No. WC8300
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
08.04.2005 (21)

Solubility in : other: inorganic solvent
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :

Method :
Year : 2000
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Remark : Formation of soluble salts in hot mixtures of HNO3 and HF
Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
Flag : Critical study for SIDS endpoint
08.04.2005 (2)

Solubility in : other: inorganic solvent
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 1993
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Remark : Tungsten carbide is insoluble in water but readily attacked by nitric acid-hydrofluoric acid mixture.
Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
18.03.2005 (19)

Solubility in : Water
Value : < 1 g/l at 18 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 2003
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
16.06.2005 (5)

Solubility in : Water
Value : < .0001 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :

Method :
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Reliability : (4) not assignable
Manufacturer data without proof
15.03.2005 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Method : Directive 92/69/EEC, A.9
Year : 2004
GLP : no data
Test substance : other TS: Tungsten carbide, purity not specified

Result : Not applicable, no flash point
Reliability : (2) valid with restrictions
Guideline study without detailed documentation
Flag : Critical study for SIDS endpoint
19.07.2005 (22)

2.8 AUTO FLAMMABILITY

Method : Directive 92/69/EEC, A.16
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Result : Auto flammability is observed. The autoignition temperature depends on the type of powder. For a commercially available powder, the observed auto ignition temperature was > 300 °C
Reliability : (2) valid with restrictions
Guideline study without detailed documentation
Flag : Critical study for SIDS endpoint
19.07.2005 (22)

2.9 FLAMMABILITY

Method : Directive 92/69/EEC, A.10
Year : 2004
GLP : no data
Test substance : other TS: tungsten carbide, purity is not specified

Result : The substance is not inflammable
Reliability : (2) valid with restrictions
Guideline study without detailed documentation
Flag : Critical study for SIDS endpoint
19.07.2005 (22)

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Carbon content

Remark : The theoretical carbon content is reported to be 6.13 % w/w.
Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
17.03.2005 (2)

Memo : Hardness

Result : Hardness of 9+ (Mohs) in solid form is reported.
Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data
Flag : Critical study for SIDS endpoint
15.03.2005 (19)

Memo : Oxidation in air

Result : Tungsten carbide is oxidized in air above 600 °C
Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data
15.06.2005 (2)

Memo : pH value

Result : At a concentration of 100 g/l of a tungsten carbide suspension in water at 20°C, a pH of 7 is reported
Reliability : (4) not assignable
Manufacturer data without proof
21.03.2005 (4)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	2005
GLP	:	
Test substance	:	
Result	:	The photodegradation of tungsten carbide cannot be calculated with the EPIWIN estimation program. The structure of the molecule is not accepted by the program. Moreover, due to the inorganic character of the substance calculations are not appropriate for the substance
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

22.12.2005 (20)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Result	:	Due to the physical-chemical properties of tungsten carbide, it is expected that the substance exists as insoluble particles in water. The water solubility was experimentally determined according to the Directive 92/69/EEC, A.6 "water solubility", comparable to OECD TG 105 (Cassella Aktiengesellschaft, 1995). Since less than 0.0001 g/l tungsten carbide is soluble in water, the substance can be regarded as insoluble in water. Furthermore, the substance is also insoluble in water and dilute acids, but forms soluble salts in hot mixtures of HNO3 and HF (Tulhoff, 2000)
Reliability	:	(2) valid with restrictions Reliable sources

22.12.2005 (21) (2)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement	:	concentration at contaminated site
Media	:	soil
Concentration	:	
Method	:	Individual particle analysis using scanning electron microscopy (SEM) with energy dispersive X-ray microanalysis (EDX)
Remark	:	Neither tungsten nor tungsten carbide concentrations determined
Result	:	In soil of the rear of a hard metal (cemented tungsten carbide) tool grinding factory elevated levels of cobalt were detected (13 g/kg soil), which decreased to 0.1-1.8 g/kg soil in the close vicinity of this factory (about 20

m away), and to the background level of 0.01-0.02 g/kg soil in the neighborhood (>= 30 m). Cobalt was closely associated with tungsten (carbon not determined), and backscatter electron micrographs indicated that some heavy metal was in the form of hard metal, consisting of tungsten carbide cemented with cobalt. Thus, cobalt contamination also points to tungsten carbide soil loads. The authors suggested that poor waste management in the factory caused the contamination of the close vicinity of this factory

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

15.06.2005 (23)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method :

Result : Traces of tungsten carbide were detected in the workplace air at several industrial facilities in the former USSR

Reliability : (4) not assignable
Original reference not translated

08.04.2005 (24)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method : SEM/EDX/AAS

Result : Metal dusts indicated the presence of cobalt in a metallic form. Cobalt tended to aggregate on tungsten carbide particles.
Almost all of the powder particles were of respirable size. Cobalt and tungsten carbide were present in dust from grinding area and other workplaces of the factory. In some areas the ratio of tungsten carbide and cobalt equalled the ratio of the raw materials, in other areas the tungsten carbide contents decreased to about 18 % w/w of the total dust, and high levels of iron oxides were detected, indicating that most of the dust was derived from a nearby iron melting factory.
Highest tungsten carbide concentration was 0.017 mg/m3.
Before shift, workers excreted less than 0.02 mg/l of cobalt in all 4 workers. Cobalt excretion peaked at 6-9 h after start of work, with peak values of 0.08 and 0.06 mg/l.
Even at low exposure levels, urinary cobalt excretion of the metal workers were higher than those of the control office workers

Test condition : - The contents of tungsten carbide and cobalt were determined at several work places in a hard metal production factory for cobalt-cemented tungsten carbide (production starts with tungsten carbide and cobalt)
- Dust was sampled at 8 workplaces for each 3 d
- For correlation of dust heavy metal conctent with urinary cobalt excretion, dust was collected by personal dust samplers equipped with glass fibre membrane filters
- Urine was sampled in 4 workers every 2 h during work
- Urinary cobalt was measured by flameless AAS
- Individual particle analysis using scanning electron microscopy (SEM) with energy dispersive X-ray microanalysis (EDX)

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

03.06.2005 (25)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	volatility
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	
Year	:	2005
Result	:	The distribution of tungsten carbide between the environmental compartments cannot be calculated with the EPIWIN estimation program, since the structure of the molecule is not accepted
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

22.12.2005 (20)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level I
Year	:	2005
Result	:	The distribution of tungsten carbide between the environmental compartments according to Mackay Level I cannot be calculated with the EPIWIN estimation program, because the structure of the molecule is not accepted
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

22.12.2005 (20)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	
Inoculum	:	other: microorganisms
Deg. product	:	
Method	:	
Year	:	2005
GLP	:	
Test substance	:	
Result	:	Due to its inertness and its low solubility in water, it is expected that tungsten carbide exists as insoluble particles in the environment. Tungsten carbide is thus not bioavailable for microorganisms for degradation, and on the other hand, not degradable due to the inorganic character of the substance. Therefore no biodegradation can be expected

Reliability : (2) valid with restrictions
Accepted calculation method
Flag : Critical study for SIDS endpoint
22.12.2005 (20)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Elimination :
Method :
Year : 2005
GLP :
Test substance : other TS: tungsten carbide

Remark : Measured bioconcentartion factors (BCF) for tungsten carbide are not available.
The structure of the substance is not accepted by the EPIWIN estimation program and therefore, a BCF is not calculable.
Flag : Critical study for SIDS endpoint
13.06.2005 (20)

3.8 ADDITIONAL REMARKS

Memo : Occupationally exposed workers in the USA

Result : According to the US National Occupational Exposure Survey from 1981 - 1983, the estimated numbers of employees potentially exposed to tungsten carbide by occupation was estimated to be 5422 (including 376 females) in the USA
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
07.04.2005 (26)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	> 1000
LC50	:	> 1000
LC100	:	> 1000
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1995
GLP	:	yes
Test substance	:	other TS: tungsten carbide, purity > 99 %
Remark	:	Accepted new scientific name for Brachydanio rerio: Danio rerio The following quality criteria were fulfilled: - the oxygen saturation was >= 60 % at the end of testing - the mortality in the control was 0 %
Result	:	Sedimentation of the test substance was observed in all test vessels. The sedimentated test substance was dispersed twice daily with an ultraturrax. The recovery rates of the active ingredient at the end of the test were > 77 %. For that reason effect level concentrations are given as nominal concentrations. A concentration-effect relationship for 24, 48, 72 and 96h was not calculated as no mortality was observed after 96h. Neither probit analysis nor graphical presentation is made. A LC50 of >1000 mg/l is derived from the test results.
Test condition	:	TEST ORGANISM: - origin: Zoo-Stumpe, 31134 Hildesheim (Germany) - length: 29 mm (n = 7/vessel) - weight: 1.6 g - medical pre-treatment: none - mortality while kept: < 5 % TEST SYSTEM: - test medium: dechlorinated drinking water, filtered and aerated for at least 24 h, hardness 82.6 CaCO3 mg/l, temperature 18.6 -21.2 °C - test vessel: aquarium with a volume of 15 l, containing 10 l test medium - natural photoperiod, light intensity 10 µmol/mE+2s - number of fish per dose: 7 - preliminary testing: range finding with 2 concentrations - application of test substance: the substance was separately weighted for each test concentration, added to the test media, and dispersed by ultrasonic for 30 min. After these treatments undissolved test substance remained in the test beakers and was dispersed twice daily with an ultraturrax 20500 rpm for 5 min. Although recoveries were 52-89 %, the nominal concentrations were used because loss of the test substance occurred during the sampling procedure. These recovery rates are attributed to the insolubility and sedimentation of the test substance in the test medium during sampling - test concentrations: 100, 180, 320, 580, 1000 mg/l. Tungsten carbide was digested with aqua regia. Tungsten was determined photometrically (at 640 nm after derivatization with 3,4-dimercaptotoluene) at test start and test end - replicate: 1 and 1 control - daily recording of non lethal and/or lethal effects

MONITORING DATA (daily):
pH range: 6.92 - 8.29
oxygen saturation: 93 - 99 %
temperature: 18.6 - 21.2 °C

Test substance : HCST product designation WC DS 100, Batch No. WC8300.
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
23.12.2005 (27)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : other: Daphnia magna STRAUSS
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : = 580
EC50 : > 1000
EC100 : > 1000
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 1995
GLP : yes
Test substance : other TS: tungsten carbide, purity > 99 %

Remark : The following quality criteria were fulfilled:
- none of the control daphnids was incapable of swimming at the end of the test or swam on the surface
- the oxygen saturation was >= 60 % (21 °C) at the end of testing

Result : The test substance was not soluble in dilution water in a concentration of 1000 mg/l. The test substance was deposited on the ground.
The recovery rates of the active ingredient at the end of the test were 67-82 % (65-78 % at start). Results are related to nominal concentrations because loss of the test substance occurred during the sampling procedure. Low recovery rates were attributed to the insolubility and sedimentation of the test substance in the test medium during sampling.
The percentage of immobility was determined in all concentration groups and controls after 24 and 48 h.
Number of daphnids incapable of swimming (immobilization) after 24 h:
- at 1000 mg/l 8 out of 80 daphnias (10 %)
- at other concentrations (32-580 mg/l, and controls) 0 out of 560 daphnias (0 %)

Number of daphnids incapable of swimming (immobilization) after 48 h:
- at 1000 mg/l 12 out of 80 daphnias (15 %)
- at 580 mg/l 8 out of 80 daphnias (10 %)
- at other concentrations (32-320 mg/l, and controls) 0 out of 480 daphnias (0 %)

EC0 values were determined directly from the test results. Effects </= 10 % are not regarded as significant for the EC0 values.
The highest concentrations that did not result in 0 % incapability of swimming during the test period were:
- 24h-EC0 = 1000 mg/l
- 48h-EC0 = 580 mg/l

None of the test concentrations resulted in 100 % incapability of swimming during the test period:
- 24h-EC100 = >1000 mg/l
- 48h-EC100 = >1000 mg/l

From the test results a 48h-EC50 of >1000 mg/l is derived.

Test condition : TEST ORGANISM:
Parthenogenetic females, cloned at the Federal Health Office (BGA), Berlin

Germany, age 2 - 24 hours
TEST SYSTEM:
- keeping water: M4 medium according to Elendt/Federal Health Office (BGA), Berlin Germany (1992)
- photoperiod: 10 hours light
- illumination: diffuse light, illumination strength 1.5 - 5 µmol*m-2*s-1
- feeding during test: none
- test vessel: glass beakers, volume 50 ml, 20 ml test medium, not ventilated, temperature 21 +/- 1 °C
- number of daphnia per beaker: 5 daphnids
- application of test substance: a stock solution of 2000 mg/l was prepared and was shaken during preparation of the test solutions. During magnetic stirring for 3 min samples were taken for analysis at the start of the experiments before addition of daphnias, and at the end of the test (determined photometrically at 640 nm after derivatization with 3,4-dimercaptotoluene)
- test concentration: 32, 58, 100, 180, 320, 580, 1000 mg/l
- number of replicate: 4 plus 1 control
- test parameter: immobilisation
MONITORING DATA (daily):
- oxygen conc. (mg/l): 9
- pH range : 7.5 - 7.9
- temperature (°C): 21.1

Test substance : HCST product designation WC DS 100, Batch No. WC8300.
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
23.12.2005 (28)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : other algae: Scenedesmus subspicatus CHODAT
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
EC0 : >= 1
EC50 : > 1
Limit test : yes
Analytical monitoring : no
Method : other: Directive 92/69/EEC, C.3, comparable to OECD TG 201
Year : 2000
GLP : yes
Test substance : other TS: tungsten carbide, purity > 99 %

Remark : Accepted new scientific name for Scenedesmus subspicatus: Desmodesmus subspicatus
The following quality criteria were fulfilled:
- the cell growth increased more than 16-fold after 72 h

Result : At a concentration of 1 mg/l no inhibition of algae growth was observed. An EC50 of >1 mg/l is derived from the test results.
Test condition : Test ORGANISM:
- stock culture: non-axenic strain obtained from the Institute of Plant Physiology at the University of Göttingen (Germany); exponentially-growing stock cultures maintained under constant temperature conditions (23 +/- 2 °C), light intensity (120 µE x m-2 x s-1); nutrient medium renewed once a week; cell density measured using a microcell counter (Sysmex F-300)
- preculture: set up three days before test started; grown under identical exposure conditions except from the use of a different nutrient medium
TEST SYSTEM:
- test vessel: 300 ml Erlenmeyer flasks with stoppers

- culturing apparatus: temperature 23 +/- 2 °C, continuous uniform illumination, shaking facility
- light intensity: 120 µE x m-2 x s-1
- dilution water: deionized water "Millipore"
- test cultures: final cell density 10E+4 cells/ml
- application of the test substance: the only test concentration of 1 mg/l was added directly to test media and then was treated with ultrasonic for 1 hour. Subsequently the dispersion was stirred on a magnetic stirrer for 24 h. Undissolved test substance was removed by filtration before adding the algae
- replicates: 3 (concentration), 6 (control)
- test parameter: growth rate/ biomass
- cell density measurement: via microcell counter (Sysmex F-300) Digitana

MONITORING DATA:
- cell density measurements of growth (daily)
- pH range: 8.0 - 10.4 (at test start, after 72 h)

Due to the insolubility of tungsten carbide in water, the analytical monitoring was omitted

Test substance : HCST product designation WC DS 100, Batch No. WC14367
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
23.12.2005 (29)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : other bacteria: Non adapted activated sludge of a predominantly domestic sewage
Exposure period : 3 hour(s)
Unit : mg/l
EC50 : > 1000
Analytical monitoring : no
Method : OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year : 1995
GLP : yes
Test substance : other TS: tungsten carbide, purity > 99 %

Remark : The following quality criteria were fulfilled:
- the two control respiration rates differ not more than 15 %
- the EC50 of the reference substance was in the accepted range (67 - 134 mg/l)

Result : The test substance was not soluble in water in a concentration of 1000 mg/l. The test substance was deposited on the ground.

Effects of the test concentration leading to an inhibition >20 % after 3h were not observed. The EC-values were not determinable. An EC50 of >1000 mg/l is derived from the test results.

Test condition : TEST ORGANISM:
- mixed population of aquatic micro-organisms of a waste water treatment plant treating predominantly domestic sewage (Hildesheim, Germany); pre-treatment: washed twice with autoclaved tap water and diluted 1:3, nutrient solution: synthetic waste water, pH 7.1, dry sludge concentration; 2.7 g/l.

TEST CONDITIONS:
- static test system
- dry sludge concentration: 2700 mg/l
- temperature: 19 °C
- test vessels: 500 ml Erlenmeyer flasks
- stirring period before start of incubation time: 16.5 h

- dispersion treatment of test substance: 15 min ultrasonic bath at 30 °C
- test concentration: 6 (58, 100, 180, 320, 580, 10000 mg/l)
- replicates: 1 per concentration and control
- test parameter: respiration rate
- aeration: permanent
- reference substance: copper (II) sulfate pentahydrate (58, 100, 180 mg/l)

MONITORING DATA:
- temperature, pH-value, oxygen

Test substance : HCST product designation WC DS 100, Lot WC8300.
Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
13.06.2005 (30)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	rat
Number of animals		
Males	:	
Females	:	3
Doses		
Males	:	
Females	:	2000 mg/kg bw
Vehicle	:	other: 1 % methyl cellulose
Route of administration	:	gavage
Exposure time	:	24 hour(s)
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1st: 2nd: 3rd:
Toxic behaviour	:	
Deg. product	:	
Method	:	other: see freetext
Year	:	2005
GLP	:	no
Test substance	:	other TS: see freetext

Method : 2 female Sprague-Dawley rats (8-12 weeks old; 216-217 g bw) received a single dose of 2000 mg/kg bw tungsten carbide (suspended in 1% methyl cellulose; 5 ml/kg bw) via gavage. One female rat served as control and received the vehicle only. Urine and faeces were collected for 24 hours after application and then the animals were sacrificed. The tungsten content in urine and faeces as well as in shaved dorsal skin, gastrointestinal tract and carcass (without skin) was determined. Tungsten was analysed by ICP-OES (Inductive coupled plasma-optical emission spectroscopy).

Result : The treatment was tolerated without clinical signs and at necropsy no pathological changes were observed. The results of the tungsten determinations are presented in the table.

Parameter/Tungsten content in milligrams (% of W found)

	/No. 1 Contr.	/No. 2 WC	/No. 3 WC
Skin	/0.0017	/ 0.0011 (.0003)	/ 0.0008 (.0002)
GIT	/0.0673	/ 4.0887 (.9805)	/ 2.3216 (.5900)
Carcass	/0.0853	/ 0.0401 (.0100)	/ 0.0557 (.0100)
Faeces	/0.1407	/412.6830 (98.97)	/393.0240 (99.36)
Urine	/0.0005	/ 0.2100 (.0500)	/ 0.1500 (.0400)
Total W	/0.2955	/417.0229	/395.5521
Total WC	/0.3150	/444.1294	/421.2630
WC dose	/0	/432.0000	/434.0000
% WC dose	/-	/103	/97

GIT= Gastrointestinal Tract

More than 98 % of the applied total tungsten found was in the faeces, about 1 % in the gastrointestinal tract, and only 0.04-0.05 % was found in the urine; this shows that after oral application of tungsten carbide to rats only a very minor part (< 0.1 %) becomes bioavailable and is excreted in urine.

Test substance : Tungsten carbide powder WC HC 240, batch no. WC 12189, purity >

99.98%.
Reliability : (2) valid with restrictions
Low number of animals tested
Flag : Critical study for SIDS endpoint
16.11.2005 (31)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : > 2000 mg/kg bw
Species : rat
Strain : other: CD
Sex : male/female
Number of animals : 5
Vehicle : other: 1 % w/v aqueous methylcellulose
Doses : 2000 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1999
GLP : yes
Test substance : other TS: see freetext

Remark : 5 animals/sex/dose; dose: 2000 mg/kg bw. TS was formulated at a concentration of 20 % (w/v) in 1 % (w/v) aqueous methylcellulose and administered by oral gavage at a dose volume of 10 ml/kg bw. The absorption of the test substance was not determined. No control animals were included in this study.
Result : Mortality: 0/5 for males and females; piloerection was observed in all rats within three minutes of dosing and persisted up to day 2; on day 2 ungroomed coat was seen in all males; recovery was complete in all rats by day 3. No changes in body weight gain and no macroscopic abnormalities at terminal kill on day 15 were observed.
Test substance : Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
31.10.2005 (32)

Type : LD50
Value : > 2000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 5
Vehicle : other: 0.8% aqueous hydroxypropyl-methylcellulose gel
Doses : 2000 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1994
GLP : yes
Test substance : other TS: purity >99%

Remark : 5 animals/sex/dose; dose: 2000 mg/kg bw. Application of 20 ml/kg bw by oral gavage; TS concentration: 10 % (w/v).
Result : Mortality: 0/5 for males and females; no clinical signs; no effects on body weight gain; no pathological findings at study termination on day 15.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
16.11.2005 (33)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 5.3 mg/l
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: no vehicle
Doses	:	5.3 mg/l
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1999
GLP	:	yes
Test substance	:	other TS: see freetext
Remark	:	5 animals/sex/concentration; concentration: 5.3 mg/l; supplied as particulate aerosol; MMAD was 7.3 µm; 48% of the particles were of a respirable size (less than 7 µm in aerodynamic diameter); snout-only exposure; control animals were exposed to clean air only.
Result	:	Mortality: 0/5 for males and females; no clinical signs; no changes in body weight gain; no pathological findings at necropsy at study termination on day 14.
Test substance	:	Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (34)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	other: CD
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: 1% w/v aqueous methylcellulose
Doses	:	2000 mg/kg bw
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1999
GLP	:	yes
Test substance	:	other TS: see freetext
Remark	:	5 animals/sex/dose; dose: 2000 mg/kg bw; 24 hours exposure; no control group was included in this study; absorption of the test substance was not determined.
Result	:	Mortality: 0/5 in males and females; no systemic or dermal response; no changes in body weight gain; no macroscopic abnormalities at study termination on day 15.
Test substance	:	Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (35)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	other: Acute toxicity test
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	no data
Year	:	1946
GLP	:	no
Test substance	:	no data
Result	:	Intraperitoneal injection of tungsten carbide to white rats did not lead to toxic symptoms; the material appeared to be inert like corundum.
Reliability	:	(4) not assignable No study details reported. No information on purity of test substance.

25.02.2005 (36)

Type	:	other: Acute toxicity test
Value	:	
Species	:	rat
Strain	:	no data
Sex	:	male
Number of animals	:	20
Vehicle	:	water
Doses	:	50 mg
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other: see freetext
Year	:	1958
GLP	:	no
Test substance	:	other TS: see freetext
Method	:	20 male rats were treated intraperitoneally with a single instillation of 50 mg tungsten carbide suspended in 0.5 ml of distilled water. After 6 months the animals were sacrificed and examined.
Result	:	Histological examination of the sacrificed animals showed no treatment-related alterations. Tungsten carbide behaved like an inert dust.
Test substance	:	No data concerning purity of substance.
Reliability	:	(4) not assignable Only limited documentation (table), no data on purity of substance.

25.02.2005 (37)

Type	:	other: Acute toxicity test
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	physiol. saline
Doses	:	
Route of admin.	:	other: intratracheal
Exposure time	:	
Method	:	no data
Year	:	1950

GLP : no
Test substance : no data

Method : Samples of tungsten carbide dust were obtained from a factory. Sterile 5 % suspensions in physiological saline were injected into the tracheae of young piebald rats under anaesthesia.
Result : Intratracheal injection of tungsten carbide yielded no unexpected results (no further details given).
Reliability : (4) not assignable
No study details reported. No information on purity of test substance.
25.02.2005 (38)

Type : other: Acute toxicity test
Value :
Species : rat
Strain : no data
Sex : male/female
Number of animals : 20
Vehicle : other: distilled water + Tween 80
Doses : 30 mg
Route of admin. : other: intratracheal
Exposure time :
Method : other: see freetext
Year : 1958
GLP : no
Test substance : other TS: see freetext

Method : 10 male and 10 female rats were treated intratracheally with a single instillation of 30 mg tungsten carbide suspended in 0.5 ml of distilled water with Tween 80. After 6 months the animals were sacrificed and examined.
Result : Histological examination of the sacrificed animals showed no treatment-related alterations. Tungsten carbide behaved like an inert dust.
Test substance : No data concerning purity of substance.
Reliability : (4) not assignable
Only limited documentation (table), no data on purity of substance.
Flag : Critical study for SIDS endpoint
25.02.2005 (37)

Type : other: Acute toxicity test
Value :
Species : mouse
Strain : NMRI
Sex : female
Number of animals :
Vehicle : physiol. saline
Doses : 2.5 mg/animal
Route of admin. : other: intratracheal
Exposure time :
Method : other: see freetext
Year : 1999
GLP : no data
Test substance : other TS: see freetext

Method : 2.5 mg of tungsten carbide was applied by intratracheal instillation (100 µl/animal in saline) to 80 mice. After 3, 15, 30 and 120 days respectively 20 animals each were sacrificed; 6 animals were used for bronchoalveolar lavage, 6 for lung homogenates, 4 for histopathology and 4 for mRNA analysis.
Result : Instillation of tungsten carbide did not induce significant changes in BALF concerning LDH-level, protein content or number of cells. Histopathological examination after 120 days revealed an accumulation of particles in the

lung parenchyma without any structural modification. The histological appearance of the lungs was similar to that of the vehicle-controls.
The level of p40 IL-12 and p70 IL-12 subunits in BALF remained unchanged whereas in lung tissue homogenate of tungsten carbide treated mice there was a transiently elevated p40 IL-12 level (significantly elevated on day 3; on day 15 back to control level).
In BAL cell cultures the levels of p40 IL-12 and p70 IL-12 were also transiently elevated on day 3.
In BAL cells the p40 IL-12-mRNA content was also elevated on day 3.
The levels of IgG1 and IgG2 in BALF remained unchanged.
Overall tungsten carbide behaved like an innocuous dust for the lung.

Test substance : Purity not mentioned; median particle diameter: 1 µm.
Reliability : (2) valid with restrictions
No data on purity of test substance
Flag : Critical study for SIDS endpoint
25.02.2005 (39)

Type : other: Intratracheal Toxicity Test
Value :
Species : rat
Strain : no data
Sex : no data
Number of animals :
Vehicle : physiol. saline
Doses : 50 mg
Route of admin. : other: intratracheal
Exposure time :
Method : other: see remark.
Year : 1967
GLP : no
Test substance : no data

Remark : Each rat received a single intratracheal application of 50 mg tungsten carbide suspended in 0.5 ml of physiological saline. A proportion of animals were sacrificed after 4, 6, and 8 months, respectively.
Result : Sacrifice after 4 months:
Lungs of killed rats showed thickening of the interalveolar septa and there was an accumulation of round cells around the bronchi and vessels.

Sacrifice after 6 months:
The cellular proliferation was more marked, especially around the vessels, and collagen fibers were observed. The walls of the small vessels were thickened and the endothelium was swollen. There was some hyperplasia of the tracheal lymph nodes, which contained free dust particles.

Sacrifice after 8 months:
Similar histologic picture as in animals after 6 months.
Reliability : (4) not assignable
No further informations on purity of test substance, on sex and number of animals per group, on incidence and severity of effects are given
16.11.2005 (40) (41)

Type : other: Intratracheal Toxicity Test
Value :
Species : rat
Strain : Sprague-Dawley
Sex : female
Number of animals :
Vehicle : physiol. saline
Doses : 10; 50; 100 mg/kg bw
Route of admin. : other: intratracheal

Exposure time :
Method : other: see freetext
Year : 1995
GLP : no data
Test substance : other TS: see freetext

Method : 8 female Sprague-Dawley rats were treated with 10, 50 or 100 mg/kg bw tungsten carbide and killed on day 1 or 28 after application. At both time points bronchoalveolar lavage was done.
Result : Only a slight increase in number of total cells, macrophages and neutrophils were observed on day 1 in the 50- and 100 mg/kg-groups. Slightly increased levels of LDH, total protein and albumin were observed on day 1 at 100 mg/kg bw in the BALF. On day 28 BAL showed no significant changes compared to the controls. No frank indication of lung fibrosis was seen.
Test substance : Purity > 99 %; 0.002 % cobalt. Median particle diameter: 2 µm.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
25.02.2005 (42)

Type : other: Intratracheal Toxicity Test
Value :
Species : rat
Strain : Sprague-Dawley
Sex : female
Number of animals :
Vehicle : physiol. saline
Doses : 10; 157 mg/kg bw
Route of admin. : other: intratracheal
Exposure time :
Method : other: see freetext
Year : 1992
GLP : no data
Test substance : other TS: see freetext

Method : 10 female Sprague-Dawley rats were instilled intratracheally with a tungsten carbide suspension of 157 mg/kg bw in physiological saline. 48 hours later animals were killed and lungs were removed.
In another experiment 5 females were treated with 10 mg/kg bw and 24 hours later bronchoalveolar lavage was performed.
Result : Histopathological examination of lungs showed that 157 mg/kg bw tungsten carbide behaved as an inert dust producing only a mild accumulation of macrophages in the alveolar duct walls. Cellular and biochemical characteristics of bronchoalveolar lavage fluid at 10 mg/kg bw were not significantly different from those of control animals.
Test substance : Purity: > 99 %; median particle diameter: 2 µm.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
25.02.2005 (43)

Type : other: Intratracheal Toxicity Test
Value :
Species : rat
Strain : Sprague-Dawley
Sex : female
Number of animals : 3
Vehicle : physiol. saline
Doses : 10 mg/kg bw
Route of admin. : other: intratracheal
Exposure time : 24 hour(s)

Method	:	other: see freetext
Year	:	1995
GLP	:	no data
Test substance	:	other TS: see freetext
Method	:	3 rats were intratracheally instilled with saline suspensions of 10 mg/kg bw tungsten carbide. 24 hours later bronchoalveolar lavage was performed and evaluated.
Result	:	Examination of bronchoalveolar lavage did not show any effect on production of inflammatory mediators and on lactate dehydrogenase activity, total protein or albumin content.
Test substance	:	Purity > 99 %; 0.002 % cobalt. Median particle diameter: 2 µm.
Reliability	:	(2) valid with restrictions Low number of animals per dose tested
Flag	:	Critical study for SIDS endpoint

25.02.2005 (44)

Type	:	other: Intratracheal Toxicity Test
Value	:	
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	15
Vehicle	:	physiol. saline
Doses	:	1 ml of 10 % solution
Route of admin.	:	other: intratracheal
Exposure time	:	
Method	:	other: see freetext
Year	:	1953
GLP	:	no
Test substance	:	other TS: see freetext
Method	:	Fifteen white rats were subjected to intratracheal instillation of 1 ml of a 10 % suspension of tungsten carbide (100 mg) in physiological saline. Rats were killed at two week intervals for a total of 18 weeks.
Result	:	After 2 weeks the test substance is concentrated in the alveoli and septal walls. After 18 weeks wider dispersal of test substance is noted but no fibrogenic response is associated with the dust accumulations. No cellular reactions other than due to an inert dust were observed.
Test substance	:	Test substance: "Pure tungsten carbide" (no further details given).
Reliability	:	(2) valid with restrictions Not all study details reported. No quantitative information on purity of test substance
Flag	:	Critical study for SIDS endpoint

03.06.2005 (45)

Type	:	other: Intratracheal Toxicity Test
Value	:	
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	physiol. saline
Doses	:	50 mg
Route of admin.	:	other: intratracheal
Exposure time	:	
Method	:	other: see freetext
Year	:	1961

GLP	:	no
Test substance	:	no data
Method	:	A suspension of 50 mg tungsten carbide in 0.5 ml saline was administered intratracheally to rats. The animals were killed 7 or 10 months later and internal organs were examined histopathologically.
Result	:	No changes were observed with exception of lungs. After 7 and 10 months slight reactions (unspecified) were observed in cells of the septa and perivascular. Stronger reactions were noted peribronchial. Only a few collagen fibers were observed after 10 months.
Reliability	:	(4) not assignable No further study details reported. No information on purity of test substance

25.02.2005 (46)

Type	:	other: Intratracheal Toxicity Test
Value	:	
Species	:	mouse
Strain	:	NMRI
Sex	:	female
Number of animals	:	
Vehicle	:	physiol. saline
Doses	:	100 mg/kg bw
Route of admin.	:	other: intratracheal
Exposure time	:	
Method	:	other: see remark
Year	:	1997
GLP	:	no data
Test substance	:	other TS: Purity > 99 %
Method	:	Female NMRI mice received a single intratracheal administration of 100 mg/kg bw tungsten carbide. Animals were sacrificed 1, 6 or 30 days post treatment and analyzed by bronchoalveolar lavage analysis for total protein content, inflammatory cell number and -type and TNF-alpha production.
Result	:	The test substance induced a mild and transient inflammatory reaction which was observed only on day 1 after instillation. tungsten carbide led to a small but not statistically significant elevation of the mean level of total protein in BALF. However tungsten carbide caused a prompt influx of polymorphonuclear leukocytes in the alveolar compartment but the total number of inflammatory cells remained unchanged compared to the control. No spontaneous release of TNF-alpha occurred at any time point in the absence of lipopolysaccharide (LPS). After LPS stimulation a reduction in TNF-alpha production on day 1 and an increase in TNF-alpha production on day 6 and 30 was observed.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (47)

Type	:	other: Intratracheal Toxicity Test
Value	:	
Species	:	mouse
Strain	:	NMRI
Sex	:	female
Number of animals	:	
Vehicle	:	physiol. saline
Doses	:	30; 100 mg/kg bw (2 applications)
Route of admin.	:	other: intratracheal
Exposure time	:	
Method	:	other: see freetext
Year	:	1998

GLP	:	no data
Test substance	:	other TS: see freetext
Method	:	Tungsten carbide was administered intratracheally to groups of each 5-10 female NMRI mice (2 doses of 0.75 and 2.5 mg/mouse; total dose ca. 60 and 200 mg/kg bw, respectively). Bronchoalveolar lavage was done 1, 3, 5, 30, 60 and 120 days after application.
Result	:	Tungsten carbide showed a noninflammatory response: No effects on plasminogen activator (urokinase), LDH-activity or total protein were observed.
Test substance	:	Purity not mentioned; median particle diameter: 1 µm; specific surface area 0.1 m2/g.
Reliability	:	(2) valid with restrictions No data on purity of test substance
Flag	:	Critical study for SIDS endpoint

25.02.2005 (48)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1999
GLP	:	yes
Test substance	:	other TS: see freetext
Remark	:	0.5 g of test substance moistened with 0.5 ml of destilled water.
Result	:	No dermal response (all animals grade 0); no clinical signs.
Test substance	:	Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (49)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	100 other: mg
Exposure time	:	72 hour(s)
Comment	:	not rinsed
Number of animals	:	3
Vehicle	:	
Result	:	slightly irritating
Classification	:	
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1999
GLP	:	yes
Test substance	:	other TS: see freetext

Remark	:	As a volume of 0.1 ml exceeded 100 mg, in accordance with protocol 100 mg were used.
Result	:	No corneal damage or iridial inflammation; diffuse crimson coloration of conjunctiva with or without slight swelling (grade 1 and 2) was seen in 2 rabbits up to 24 hours; in the remaining rabbit chemosis grade 1 was observed only 1 hour after instillation; 48 hours after instillation all ocular reactions had resolved. Tungsten carbide showed only a transient very slight to well-defined conjunctival irritation. Based on the results of this study, tungsten carbide can be considered as non-irritant.
Test substance	:	Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (50)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1st: Induction 50 % intracutaneous 2nd: Induction 75 % occlusive epicutaneous 3rd: Challenge other: 37.5 and 75 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	other: Alembicol D (fractionated coconut oil)
Result	:	not sensitizing
Classification	:	
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1999
GLP	:	yes
Test substance	:	other TS: see freetext
Remark	:	Negative control group consisted of 5 animals. No simultaneous positive control. The sensitivity of the guinea pig strain used is checked periodically with known sensitizers hexyl cinnamic aldehyde (HCA), benzocaine and 2-mercaptobenzothiazole (MBT).
Result	:	At challenge no dermal responses were observed in any of the 10 animals; no clinical signs.
Test substance	:	Tungsten carbide powder WC HC 240, batch no. WC 12189, purity > 99.98%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

16.11.2005 (51)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	6 days
Doses	:	0.015 mg/l
Control group	:	yes
LOAEL	:	= .015 mg/l
Method	:	other: see remark

Year : 1986
GLP : no data
Test substance : other TS: purity >99.4%

Remark : Test substance supplied as aerosol; MMAD = 4.2 µm with geometric standard deviation of 1.86; whole-body exposure; monitoring of test substance concentrations in exposure chambers (analytical: 14.97 mg/m3; this value was not statistically different to the nominal concentration of 15 mg/m3).
Control group was exposed to filtered air.
The objective of study was to relate a series of functional tests to compositional and structural alterations in the rat lung, induced by exposure to tungsten carbide and cobalt dusts (here, only exposure to tungsten carbide is considered). For the study with cobalt a concentration of 1 mg/m3 was selected based on previous animal data showing a clear effect at this exposure level. Due to the fact that the ratio of cobalt to tungsten carbide in hard metal is usually 1 to 15 the tungsten carbide concentration used for this test was 15 mg/m3.
24 male rats were designated for respiratory physiology studies (parameters of spontaneous breathing, electrocardiographic data, lung volumes, parenchymal behaviour, distribution of ventilation, flow volume dynamics). After pulmonary testing these animals were sacrificed and the left lung was processed for pathological examination while the right lung was submitted for biochemical analysis (weight, water content, protein, DNA, elastin, collagen). 8 rats/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs examined). Another 10 male rats were designated for cytogenetic and sperm abnormalitiy studies (these endpoints have not been evaluated).

Result : After exposure to tungsten carbide, the pulmonary function tests showed no evidence of fibrogenic (restrictive) processes nor was there any indication of an obstructive lung disease. Similarly, hematological indices showed no effects. Protein and DNA content of lungs was slightly decreased when expressed in terms of dry lung weight. The lesions observed in the lungs of tungsten carbide exposed rats consisted of focal reactions around the end-airways and their proximal alveoli. Minimal to moderate alveolar wall thickening with type II cell hyperplasia and accumulations of pigmented macrophages were characteristic. Although chronic rhinitis was not detected in any of the female rats, the incidence in male rats appeared to be related to tungsten carbide exposure. This change was characterized by submucosal infiltration of mononuclear cells in the nasal cavity. Occasional lesions in non-respiratory tissues all appeared to be spontaneous.
The LOEL was at 15 mg/m3 based on mild histopathological alterations in the lungs (focal reactions around the end airways) and chronic rhinitis in males.

Reliability : (2) valid with restrictions
Only one concentration tested
Flag : Critical study for SIDS endpoint
16.11.2005 (52)

Type : Sub-chronic
Species : rat
Sex : no data
Strain : other: white

Route of admin.	:	inhalation
Exposure period	:	5 months
Frequency of treatm.	:	daily for one hour
Post exposure period	:	no
Doses	:	0.6 mg/l
Control group	:	yes
LOAEL	:	= .6 mg/l
Method	:	other: see freetext
Year	:	1967
GLP	:	no
Test substance	:	other TS: see freetext

Method : White rats were whole body exposed for 1 hour daily over a period of 5 months to 600 mg/m3 tungsten carbide dust. The animals were sacrificed after the last exposure and examined. A control group is mentioned but no details given.

Result : Animals remained healthy and gained body weight well. No macroscopic changes were detected. On microscopical examination no changes were found in any organ except for the lungs, where perivascular and peribronchial infiltration were observed. The walls of some of the small vessels were thickened, with loose fibers and a swollen endothelium. The interalveolar septa were thickened, due to the proliferation of lymphoid-histiocytic elements. Dust particles, mainly located intracellularly, surrounded the vessels and were also found in the interalveolar septa.

Test substance : Purity not given. Up to 77 % of the particles were smaller than 5 µm.

Reliability : (4) not assignable
No further study details reported. No information on purity of test substance

Flag : Critical study for SIDS endpoint

03.06.2005 (40) (41)

Type	:	Sub-acute
Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	other: intratracheal
Exposure period	:	4 months
Frequency of treatm.	:	monthly
Post exposure period	:	1 month
Doses	:	10 mg/kg bw
Control group	:	yes, concurrent vehicle
Method	:	other: see freetext
Year	:	1995
GLP	:	no data
Test substance	:	other TS: see freetext

Method : 15 females were instilled with 10 mg/kg bw monthly over a period of 4 months. Evaluation of bronchoalveolar lavage fluid (BALF) and histopathological examinations of the lung were done 1 month after last treatment.

Result : No alterations of biochemical or cellular parameters or lung hydroxyproline content could be observed. Histopathology of the lung revealed no difference to sections of controls except for the presence of fine black particles deposited in alveolar macrophages.

Test substance : Purity > 99.9 %; 0.002 % cobalt. Median particle diameter: 2 µm.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

11.07.2005 (42)

Type : Sub-chronic

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 hours/day, 5 days/week
Post exposure period	:	6 days
Doses	:	0.015 mg/l
Control group	:	yes
LOAEL	:	= .015 mg/l
Method	:	other: see remark
Year	:	1986
GLP	:	no data
Test substance	:	other TS: purity >99.4%

Remark : Test substance supplied as aerosol; MMAD = 4.2 µm with geometric standard deviation of 1.86; whole-body exposure; monitoring of test substance concentrations in exposure chambers (analytical: 14.97 mg/m3; this value was not statistically different to the nominal concentration of 15 mg/m3).
Control group was exposed to filtered air.
The study with mice was run parallel to the study with F344 rats using the same exposure concentration. 8 mice/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs tested), but no functional tests of the lungs were conducted. Another 10 male mice were designated for cytogenetic and sperm abnormalitiy studies (these endpoints have not been evaluated).

Result : Animals did not demonstrate marked lung lesions, although the females had chronic rhinitis. No other organ lesions could be attributed to the treatment with tungsten carbide. The LOEL was at 15 mg/m3 based on chronic rhinitis in females.

Reliability : (2) valid with restrictions
Only one concentration tested

Flag : Critical study for SIDS endpoint

16.11.2005 (52)

Type	:	Sub-acute
Species	:	guinea pig
Sex	:	no data
Strain	:	no data
Route of admin.	:	other: intratracheal
Exposure period	:	
Frequency of treatm.	:	weekly
Post exposure period	:	12 months after last application
Doses	:	3 x 50 mg
Control group	:	
Method	:	other: see freetext
Year	:	1955
GLP	:	no
Test substance	:	other TS: see freetext

Method : A mixture of tungsten carbide and carbon (ratio 94:6) was suspended in isotonic saline and instilled into lungs of 6 guinea pigs (600 g bw). A total dose of 150 mg (250 mg/kg bw) was administered in three equal parts at weekly intervals and guinea pigs were followed up for 30-360 days.

Result : The immediate response was diffuse hyperemia with bronchial catarrh. 30 days after treatment focal interstitial pneumonitis and lymphoid hyperplasia was noted with almost complete recovery after 1 year. After 1 year trapped dust masses and

subpleural fibrocellular granulomata were observed.

Reliability : (4) not assignable
No further study details reported. Mixed exposure to tungsten, tungsten carbide and carbon with no information on the purity, physical nature or particle size of the test materials.

16.11.2005 (53) (54) (55)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : other: alkaline comet-assay in-vitro
System of testing : human lymphocytes
Test concentration : 10, 20, 75 and 100 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : ambiguous
Method : other: see remark
Year : 1997
GLP : no data
Test substance : other TS: purity: 99.5%, median particle size < 1µm

Remark : Human lymphocytes were incubated for 15 minutes at 37°C. The cells came from healthy human individuals. No repetition of experiments was done. Only 50 cells/concentration were evaluated.
Result : No cytotoxicity was observed. Exposure of human lymphocytes up to 100 µg/ml did not induce changes in tail length or tail moment compared to controls. Nevertheless treated cells presented a relatively higher DNA content in the tail at 75 and 100 µg/ml than control comets. This elevation was only slight and not dose-dependent.
Test substance : Median particle size: < 1 µm.
Reliability : (2) valid with restrictions
No repetition of experiments was done. Only 50 cells/concentration were evaluated.
Flag : Critical study for SIDS endpoint
25.02.2005 (56)

Type : other: alkaline elution
System of testing : human lymphocytes
Test concentration : 25, 50, 100 and 250 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: see remark
Year : 1997
GLP : no data
Test substance : other TS: purity: 99.5%, median particle size < 1µm

Remark : Human lymphocytes, labelled with 1 µCi/ml of [methyl-3H]-thymidinetriphosphate, were incubated for 10 and 20 minutes respectively with tungsten carbide at 37°C. The cells came from healthy human individuals. No repetition of experiments was done.
Result : Treatment of cells up to 250 µg/ml did not induce more DNA breaks than observed in controls. There was no cytotoxicity at any concentration.
Test substance : Median particle size: < 1 µm.
Reliability : (2) valid with restrictions
No independent repeat experiment performed
Flag : Critical study for SIDS endpoint
25.02.2005 (56)

Type : other: alkaline comet-assay in-vitro
System of testing : human lymphocytes
Test concentration : 10, 50, 75 and 100 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : ambiguous
Method : other: see remark
Year : 1997
GLP : no data
Test substance : other TS: purity: 99.5%, median particle size < 1µm

Remark : Human lymphocytes prepared from peripheral blood of a single healthy volunteer were incubated with tungsten carbide for 15 minutes at 37°C. No repetition of experiments was done. Only approx. 50 cells/concentration were analysed.
As a measure for cell cycle delay and/or cytotoxicity the relative division index (RDI) was used.

Result : The test substance induced slight but significant increases in tail length and tail moment in all concentrations tested. This effect showed no dose-dependency.

Table: DNA migration in isolated human leukocytes

Group	/Conc.°/cells/mean TL (SD)	/mean TM (SD)	/RDI
Neg.Contr./-	/44	/18.8 (10.9)	/ 2.50 (2.1) /100
WC	/10	/49	/29.1 (19.3)** / 6.90 (10.8)* /95
	/50	/49	/25.2 (17.1)** / 6.90 (11.2)***/73
	/75	/96	/25.1 (14.5)***/ 5.10 (8.0)** /88
	/100	/73	/25.4 (13.8)***/ 5.30 (6.3)** /68
Pos.Contr./242	/48	/56.6 (11.7)***/18.90 (10.6)***/nd (EMS)	

°) in µg/ml
(SD) +/- standard deviation nd: not determined
TL: Tail length (µm) TM: Tail moment
RDI=Relative division index
*) P < 0.05
**) P < 0.01
***) P < 0.0001

Test substance : Median particle size: < 1 µm.
Reliability : (2) valid with restrictions
No repetition of experiments was done. Only 50 cells/concentration were evaluated.
Flag : Critical study for SIDS endpoint
25.02.2005 (57)

Type : other: Micronucleus in-vitro
System of testing : human lymphocytes
Test concentration : 10, 50, 75 and 100 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : ambiguous
Method : other: see freetext
Year : 1997
GLP : no data
Test substance : other TS: purity: 99.5%, median particle size < 1µm

Method : Two lymphocyte cultures/concentration from the same donor were analysed to evaluate micronucleus induction. Cells were stimulated to divide by 24 hr treatment with phytohaemagglutinin. Cells were incubated with tungsten carbide for 15 minutes at 37 °C and then further incubated for

a total of 72 hrs. After 44 hrs cytochalasin B was added to block cytokinesis. No repetition of experiments was done. Mitomycin C was used as positive control (48 hrs exposure). Duplicate cultures were analysed for each concentration tested. 1000 cytokinesis-blocked cells/culture were analysed. As a measure for cell cycle delay and/or cytotoxicity the relative division index (RDI) was used.
The method is with some important exceptions (especially: no independent repeat) comparable to the draft OECD TG 487.

Remark : Metal particles were removed by using a magnetic source. It is unclear whether this procedure was also used for the assay with tungsten carbide particles and whether the magnetic source was used for the negative control also since magnetic fields alone have been reported to be also able to induce chromosomal damages in lymphocytes.

Result : A statistically significant, but not dose-dependent increase in micronuclei was observed at 50, 75 and 100 µg/ml. A decrease of the percentage of cytokinesis-blocked cells and of the relative division index (RDI) was observed at the highest concentration of 100 µg/ml which can either be a sign of cytotoxicity or of cell cycle delay.

Table: Micronucleus induction in isolated human leukocytes

Group	/Conc.°/	Culture/CB % /% MNCB/% MNCB (mean)/RDI
Neg.Control	/-	/1 /33.7 /1.0 /
	/-	/2 /32.1 /1.1 /1.05 (0.07) /100
WC	/10	/1 /27.9 /1.5 /
	/10	/2 /34.4 /1.2 /1.35 (0.21) /95
	/50	/1 /27.5 /2.3 /
	/50	/2 /21.1 /2.7 /2.50 (0.28)* /73
	/75	/1 /31.7 /1.9 /
	/75	/2 /26.4 /2.4 /2.15 (0.35)* /88
	/100	/1 /22.3 /2.4 /
	/100	/2 /22.8 /2.3 /2.35 (0.07)* /68
Pos.Control (MMC)	/0.15	/1 /30.3 /8.7 /
	/0.15	/2 /39.4 /7.7 /8.20 (0.71)**/105

°) in µg/ml
() +/- standard deviation
*) P < 0.01
**) P < 0.0001
CB=Cytokinesis-blocked cells
MNCB=Micronucleated cytokinesis-blocked cells
RDI=Relative cell division index

Test substance : Median particle size: < 1 µm.

Reliability : (2) valid with restrictions
No independent repeat experiment performed (only one donor used; draft OECD TG 487 recommends use of two donors). Percentage of binucleated cells in control group only ca. 33 % (Draft OECD TG 487 recommends 50 %). Treatment time only 15 minutes (Draft OECD TG 487 recommends 3-6 hrs). No historic control data available. Unclear impact of magnetic source on result.

Flag : Critical study for SIDS endpoint

08.07.2005 (57)

Type : Ames test

System of testing : Salmonella typhimurium TA98, TA100, TA1535, TA1537 and E. coli WP2uvrA/pKM101

Test concentration : 5, 15, 50, 150, 500, 1500, 5000 µg/plate

Cycotoxic concentr. :

Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 471

Year : 2001

GLP : yes
Test substance : other TS: purity > 99.8%

Remark : 2 independent tests performed: range-finding (standard plate incorporation assay) and repeat (including a pre-incubation stage). Rat liver S9 mix was prepared from rats after pretreatment with Aroclor 1254.
Result : No signs of toxicity towards any of the tested strains at any dose. No substantial increase in revertant colony numbers over control counts were obtained with any of the tester strains at any tungsten carbide concentration in either the presence or the absence of S9 mix. The positive controls were functional.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
16.11.2005 (58)

Type : Cytogenetic assay
System of testing : Human lymphocytes
Test concentration : 2.44; 4.88; 9.77; 19.53; 39.06; 78.13; 156.25; 312.5 µg/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : OECD Guide-line 473
Year : 2001
GLP : yes
Test substance : other TS: purity > 99.8 %

Remark : Human lymphocytes were prepared from blood from healthy donors. Lymphocytes were incubated with tungsten carbide for 3 hours with and without rat-liver S9-mix (first test), then washed and further incubated for 17 hours for recovery. In the second test incubation was continuously for 20 hours without S9 mix or for 3 hours with rat-liver S9-mix like in the first test.
Tungsten carbide was suspended in culture medium. The suspension showed precipitates at 312.5 µg/ml. Because of precipitation of the substance at 312.5 µg/ml, this concentration was selected as the highest test dose. No cytotoxicity was found at this dose. Mitotic indices were determined for 1000 cells; metaphase analysis was performed for 100 cells. Polyploidy was analysed for 500 cells each of untreated control and highest tungsten carbide concentration tested.
Result : Two separate tests were performed.
In both tests no cytoxicity of tungsten carbide was observed towards human lymphocytes. There was no increase in the number of polyploid metaphase cells compared to the solvent control.
First test:
Without S9 mix: no biologically relevant increases of chromosomal aberrations at any tungsten carbide concentration.

Exp.[h]/WC[µg/ml]/CA-gaps[%]/CA+gaps[%]/RMI[%]/Polyploidy
3 /0 /3;2;2.5 /5;3;4.0 /100 /0.1 %
3 /78.13 /3;5;4.0 /7;7;7.0 /87 /nd
3 /156.25 /2;5;3.5 /7;9;8.0 /98 /nd
3 /312.5 /7;4;5.5 /11;8;9.5 /92 /0.0 %
3 /MMC /31.0* /34.0* /- /nd
*) P < 0.001

With S9 mix: statistically singnificant increase in number of chromosomal aberrations at 78.13 and 156.25 µg/ml when compared to solvent control. No reproducible values were observed between replicate cultures at 78.13 µg/ml. However, cultures exposed to tungsten carbide contained cells with a frequency of aberrations (excluding gaps) that exceeded the upper 99 % limit of the historical negative control range (3.34 %, mean 0.84 %) at dose

levels of 78.13 µg/ml and above.

Exp.[h]/WC[µg/ml]/CA-gaps[%]/CA+gaps[%] /RMI[%]/Polyploidy
3 /0 /3;3;3.0 /4;5;4.5 /100 /0.0 %
3 /78.13 /7;16;11.5*/8;17;12.5**/113 /nd
3 /156.25 /9;8;8.5** /11;9;10.0 /89 /nd
3 /312.5 /8;5;6.5 /10;6;8.0 /100 /0.1 %
3 /CPA /26.0* /29.0* /- /nd
*) P < 0.001 **) P < 0.01

Second test:
Without S9 mix: no biologically relevant increases of chromosomal aberrations at any tungsten carbide concentration.

Exp.[h]/WC[µg/ml]/CA-gaps[%]/CA+gaps[%]/RMI[%]/Polyploidy
20 /0 /2;2;2.0 /4;2;3.0 /100 /0.1 %
20 /78.13 /4;8;6.0 /8;10;9.0**/111 /nd
20 /156.25 /6;2;4.0 /7;7;7.0 /104 /nd
20 /312.5 /4;6;5.0 /4;9;6.5 /87 /0.0 %
20 /MMC /25.5* /28.5* /- /nd
*) P < 0.001 **) P < 0.01

With S9 mix: no statistically singnificant increase in number of chromosomal aberrations at any tungsten carbide concentration.

Exp.[h]/WC[µg/ml]/CA-gaps[%]/CA+gaps[%]/RMI[%]/Polyploidy
3 /0 /3;3;3.0 /3;3;3.0 /100 /0.0 %
3 /78.13 /2;5;3.5 /4;6;5.0 /112 /nd
3 /156.25 /9;4;6.5 /10;6;8.0 /96 /nd
3 /312.5 /5;5;5.0 /7;5;6.0 /101 /0.1 %
3 /CPA /20.0* /26.0* /- /nd
*) P < 0.001

However, the statistical significance was decreased due to high solvent control values (mean = 3 % excluding gaps) and cultures exposed to tungsten carbide at the two highest concentrations contained cells with a frequency of aberrations (excluding gaps) that exceeded the upper 99 % limit of the historical negative control range (3.34 %, mean 0.84 %). The positive controls were functional.

The author concludes that there is no evidence of clastogenic activity in the absence of S9 mix and that there is equivocal evidence of clastogenic activity in the presence of S9 mix.

Test substance : Tungsten carbide powder DS 100; batch no. WC15091.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
16.11.2005 (59)

Type : other: Alkaline Comet Assay
System of testing : Human lymphocytes (peripheral blood mononucleated cells)
Test concentration : 10, 50, 100 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: see remark
Year : 1988
GLP : no data
Test substance : other TS: Purity > 99 %

Method : Isolated human lymphocytes were incubated with tungsten carbide for 15

min at 37°C. The Comet assay was performed according to the method of Singh et al. 1988.

Remark : Surface area of tungsten carbide: 1.003 m2/g
Median diameter: 1.0 µm.

Result : Tungsten carbide did not induce significant DNA migration in human lymphocytes from two donors.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

25.02.2005 (60)

Type : Micronucleus test in vitro
System of testing : Human lymphocytes (peripheral blood mononucleated cells)
Test concentration : 10, 50, 100 µg/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: see remark
Year : 1985
GLP : no data
Test substance : other TS: Purity > 99 %

Method : Isolated human lymphocytes from two donors were incubated with tungsten carbide for 15 min at 37°C. The micronucleus assay was performed according to the method of Fenech and Morley 1985. The method is with some minor exceptions comparable with the draft OECD TG 487.

Remark : Surface area of tungsten carbide: 1.003 m2/g
Median diameter: 1.0 µm.

Result : Tungsten carbide did not induce significant elevations in micronucleated cells.

Reliability : (1) valid without restriction
Independent repeat experiment was performed (two donors). Percentage of binucleated cells in control group only ca. 38 % (Draft OECD TG 487 recommends 50 %). Treatment time only 15 minutes (Draft OECD TG 487 recommends 3-6 hrs). No historic control data available

Flag : Critical study for SIDS endpoint

08.07.2005 (60)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : other: subchronic inhalation toxicity
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 13 weeks
Frequency of treatm. : 6 hours/day, 5 days/week
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 0.015 mg/l

Control group : yes
Result : negative
Method : other: see remark
Year : 1986
GLP : no data
Test substance : other TS: purity >99.4%

Remark : Test substance supplied as aerosol; MMAD = 4.2 µm with geometric standard deviation of 1.86; whole-body exposure; monitoring of test substance concentrations in exposure chambers (analytical: 0.01497 mg/l; this value was not statistically different to the nominal concentration of 0.015 mg/l).
Control group was exposed to filtered air.
The objective of study was to relate a series of functional tests to compositional and structural alterations in the rat lung, induced by exposure to tungsten carbide and cobalt dusts (here, only exposure to tungsten carbide is considered). For the study with cobalt a concentration of 1 mg/m3 was selected based on previous animal data showing a clear effect at this exposure level. Due to the fact that the ratio of cobalt to tungsten carbide in hard metal is usually 1 to 15 the tungsten carbide concentration used for this test was 15 mg/m3.
24 male rats were designated for respiratory physiology studies (parameters of spontaneous breathing, electrocardiographic data, lung volumes, parenchymal behaviour, distribution of ventilation, flow volume dynamics). After pulmonary testing these animals were sacrificed and the left lung was processed for pathological examination while the right lung was submitted for biochemical analysis (weight, water content, protein, DNA, elastin, collagen). 8 rats/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs examined including uterus, ovaries, testes, epididymides and prostate). Another 10 male rats were designated for cytogenetic and sperm abnormalitiy studies (these endpoints have not been evaluated).

Result : After exposure to tungsten carbide, the pulmonary function tests showed no evidence of fibrogenic (restrictive) processes nor was there any indication of an obstructive lung disease. Similarly, hematological indices showed no effects. Protein and DNA content of lungs was slightly decreased when expressed in terms of dry lung weight. The alterations observed in the lungs of tungsten carbide exposed rats consisted of focal reactions around the end-airways and their proximal alveoli. Minimal to moderate interstitial thickening, type II cell hyperplasia and accumulations of pigmented macrophages were characteristic. Occasional lesions in non-respiratory tissues including testes, epididymides, prostata, uterus and ovary, all appeared to be spontaneous.

Reliability : (2) valid with restrictions
Only one concentration tested

Flag : Critical study for SIDS endpoint
16.11.2005 (52)

Type : other: subchronic inhalation toxicity
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : inhalation
Exposure period : 13 weeks

Frequency of treatm.	:	6 hours/day, 5 days/week
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	0.015 mg/l
Control group	:	yes
Result	:	negative
Method	:	other: see remark
Year	:	1986
GLP	:	no data
Test substance	:	other TS: purity >99.4%
Remark	:	Test substance supplied as aerosol; MMAD = 4.2 µm with geometric standard deviation of 1.86; whole-body exposure; monitoring of test substance concentrations in exposure chambers (analytical: 0.01497 mg/l; this value was not statistically different to the nominal concentration of 0.015 mg/l). Control group was exposed to filtered air. The study with mice was run parallel to the study with F344 rats using the same exposure concentation. 8 mice/sex were designated for observation of body weight changes, organ weights, hematology and pathology (34 organs tested including uterus, ovaries, testes, epididymides and prostate), but no functional tests of the lungs were conducted. Another 10 male mice were designated for cytogenetic and sperm abnormalitiy studies (these endpoints have not been evaluated).
Result	:	Animals did not demonstrate marked lung lesions, although the females had rhinitis which may have been related to overall dust exposure. No lesions in other organs including testes, epididymides, prostata, uterus and ovary could be attributed to the treatment.
Reliability	:	(2) valid with restrictions Only one concentration tested
Flag	:	Critical study for SIDS endpoint

16.11.2005 (52)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience	:	other: Occupational Disease Regulation
Remark	:	Occupational Disease No. 4107 in Germany
Result	:	Disease of pulmonary fibrosis caused by metal dusts at production or processing of hard metals is officially recognized as an occupational disease in Germany. (Hard metals usually consist of tungsten carbide mixed with

cobalt, titanium, nickel, tantalum, chromium etc.).

Reliability : (4) not assignable
Medical review on hard metal disease
25.02.2005 (61)

Type of experience : other: Review

Remark : Review: "Heart disease, cor pulmonale"
Result : Tungsten carbide is said to be a documented cause of chronic cor pulmonale (heart failure caused by lung disease), though there does not exist any prevalence data. (No information about probable co-exposure with cobalt is given.)
Reliability : (4) not assignable
25.02.2005 (62)

Type of experience : other: Review

Remark : Review: "Metal Toxicity and Respiratory Tract"
Result : Hard metal lung disease is a fibrosis characterized by desquamative and giant cell interstitial pneumonitis and is probably caused by cobalt, since a similar disease has been observed in diamond polishers who used polishing discs made with microdiamonds (not tungsten carbide) cemented with cobalt. On the other hand, no lung fibrosis has been reported in workers involved in the mining or refining of cobalt.
Reliability : (4) not assignable
25.02.2005 (63)

Type of experience : other: Review

Remark : Review: "Respiratory Tract Disease"
Result : Tungsten carbide dust can cause a syndrome of pulmonary fibrosis with manifestations of restrictive disorder to a progressive loss of lung volume. These syndromes are called hard-metal disease and are believed to be due to an idiosyncratic reaction to cobalt in tungsten carbide dust.
Reliability : (4) not assignable
25.02.2005 (64)

Type of experience : other: Review

Remark : Review: "Chronic lung disease, Pulmonary Fibrosis"
Result : Tungsten carbide is highly fibrogenic leading to pulmonary fibrosis called hard metal disease. (No information about probable co-exposure with cobalt is given.)
Reliability : (4) not assignable
25.02.2005 (65)

Type of experience : other: Review

Remark : Review: "Other Pneumoconioses"
Result : Much experimental work suggests that cobalt is the responsible agent for both interstitial and obstructive syndromes of respiratory disease in tungsten carbide workers.
Reliability : (4) not assignable
25.02.2005 (66)

Type of experience : other: Case Studies

Remark : Case studies of hard metal disease were mostly not added to this IUCLID because of co-exposure with cobalt or unclear exposure conditions.
01.02.2005

Type of experience : other: Review

Remark : Review: "Pulmonary reaction to other occupational dusts and fumes"
Result : Hard metal is defined as tungsten carbide combined with cobalt. While tungsten carbide was found to be relatively inert in animal experiments, cobalt is highly expected as the agent responsible for hard metal disease.
Reliability : (4) not assignable
25.02.2005 (67)

Type of experience : other: Review

Remark : Review: "Human Toxicity of Cobalt-Containing Dust"
Result : A review of clinical and epidemiological studies indicates that the risk of developing a fibrosing alveolitis which is a syndrome of hard metal disease only occurs when cobalt metal is inhaled in association with other dusts such as tungsten carbide.
Reliability : (4) not assignable
25.02.2005 (68)

Type of experience : other: Review

Remark : Review: "Chronic bronchitis and emphysema"
Result : Tungsten carbide is considered to be a probable causative agent for chronic bronchitis. (No information about probable co-exposure with cobalt is given.)
Reliability : (4) not assignable
25.02.2005 (69)

Type of experience : other: Review

Remark : Review: "The pneumoconioses"
Result : Hard metal disease is described to be a form of pneumoconiosis with manifestation of interstitial fibrosis. Tungsten carbide is considered to be the causative agent. (No information about probable co-exposure with cobalt is given.)
Reliability : (4) not assignable
25.02.2005 (70)

Type of experience : other: Review

Remark : Review: "Interstitial fibrosis due to hard metals"
Result : In animal experiments, only cobalt, not tungsten carbide, shows a particular toxicity and possibly sensitization potential.
Reliability : (4) not assignable
25.02.2005 (71)

Type of experience : other: Review

Remark : Review: "Some Important Occupational Lung Diseases"
Result : Tungsten carbide, known as hard metal in industry, is produced by a process of powder metallurgy from tungsten

carbide with cobalt as a binder. Exposure leads to interstitial fibrosis, of which cobalt is believed to be the responsible agent.

Reliability : (4) not assignable
25.02.2005 (72)

Type of experience : other: Review

Remark : Review: " Pulmonary reactions to miscellaneous mineral dusts, man-made mineral fibers, and miscellaneous pneumoconioses"

Result : NIOSH recommended that exposure to tungsten carbide with more than 2% cobalt should be limited to current standards for cobalt exposure.

Reliability : (4) not assignable
25.02.2005 (73)

Type of experience : other: Review

Remark : NIOSH: criteria for a recommended standard; occupational exposure to tungsten and cemented tungsten carbide

Reliability : (4) not assignable
25.02.2005 (74)

Type of experience : other: Review

Remark : Review: "The hard metal diseases"

Result : Symptoms of hard metal disease are described and include asthma, hypersensitivity lung disease (also known as allergic alveolitis) and pulmonary fibrosis. Cobalt is considered to be the causative agent.

Reliability : (4) not assignable
25.02.2005 (75)

Type of experience : other: Case Report

Result : A 42 year old male worker was exposed to tungsten carbide dust from 1958 to 1977. In 1972 he suffered from cough with mucous sputum and dyspnea. The symptoms disappeared after the man had stopped working for a while. The radiography of the lung showed a discrete reticulomicronodular picture without any other pathological changes. In 1977 he suffered again from chronic coughing with mucous sputum. The radiography of the lung showed a diffuse reticulomicronodular picture without any other pathological changes. Lung function tests showed a discrete restrictive syndrome without obstructive troubles. After 9 months of absence from work the symptoms had disappeared but the results from lung function tests were unchanged (no informations on cobalt exposure given).

Reliability : (2) valid with restrictions
No quantitative informations on exposure, no informations about possible coexposure to cobalt
25.02.2005 (76)

Type of experience : other: Case Report

Remark : No workplace air concentrations were reported.

Result : 12 persons working in the manufacture or grinding of tungsten carbide developed a progressive diffuse interstitial pneumonia characterized clinically by nonproductive cough and by dyspnea on exertion. Microscopic examination of lung tissue of 9 persons showed interstitial infiltrates of mononuclear and mast cells, desquamated histiocytes in the alveoli and various amounts of interstitial fibrosis. 8 persons have died and 5 additional persons with episodic cough related to dust exposure but without roentgen

anomalies in the lung have been observed.
Tungsten carbide was detected in the lungs of 5 workers employed in the manufacture or grinding of cemented tungsten carbide ("hard metal"). Mass spectrometry of the lungs of three of them showed additionally the presence of cobalt and in one case also of titanium. In the lung of this person the content of tungsten, titanium and cobalt was 3.0, 2.0, and 0.1 µg/g wet lung weight, respectively. The available evidence indicates that this disease is a pneumoconiosis related to inhalation of finely powdered cobalt.

Reliability : (2) valid with restrictions
03.06.2005 (77)

Type of experience : other: Case Report

Result : A 45 year old man who had been exposed for several years to dusts consisting of tungsten carbide, silicon carbide and aluminium oxide at the workplace suffered from an extrinsic asthma. It is assumed that the symptoms were due to simultaneous exposure to cobalt which is a component of hard metal dust.

Reliability : (2) valid with restrictions
No quantitative informations on exposure
14.03.2005 (78)

Type of experience : other: Case Report

Result : 9 of about 1500 workers in a tungsten carbide manufacturing plant have demonstrated a respiratory sensitization syndrome characterized by cough, chest tightness, wheezing, and in 3 of the 9 individuals also itching of the skin. Due to the lack of reaction to pure tungsten and the high reactivity towards pure cobalt dust the symptoms have been evolved obviously due to simultaneous exposure to cobalt dust.

Reliability : (2) valid with restrictions
No quantitative informations on exposure
25.02.2005 (79)

Type of experience : other: Biological Monitoring

Method : - 33 workers from 3 factories producing either diamond tools (group A, n=10; group B, n=11) or hard-metal inserts (group C, n=12)
- Groups A and B were exposed either to Co and WC powders, which were mixed to produce hard-metal alloys, or to metal dust originating from dry-grinding activities
- Group C was exposed to metal dust produced during the dry grinding of hard-metal pieces
- Contol group of 16 adult healthy subjects, not occupationally exposed to metals
- Exhaled breath condensate (EBC), a fluid formed by cooling exhaled air, was used to assess target tissue dose and effects of inhaled cobalt and tungsten carbide

Remark : Discrepancies regarding group size between text (A, n=12; C, n=10) and tables (A, n=10; C, n=12).

Result : Airborne concentrations (mg/m³) of cobalt and tungsten [median (range)] were measured in the three workplaces:

Group	Cobalt	Tungsten
A	8.25 (0.1 - 16.4)	<0.01
B	8.45 (0.9 - 16.0)	0.10 (0.01 - 0.2)
C	26 (14.6 - 37.4)	3 (1.1 - 4.9)

The highest concentration of tungsten (with most of it probably in the form of tungsten carbide) was 4.9 mg/m³ air, but most values were at least one order of magnitude lower.

The tungsten content in EBC of exposed workers ranged from < 0.5 to 25.6 nmoles/liter. In urine the tungsten content ranged between < 0.06 to 8.2 µmol/mol creatinine. EBC was suitable for simultaneous determination of contents of cobalt, tungsten and MDA as a biomarker for pulmonary oxidative stress; all these parameters were correlated.

Table: Cobalt and tungsten in air, EBC and urine of workers at end of shift in 3 different working environments

Variables	/Control	/Group A	/Group B	/Group C
No. of workers/16		/10	/11	/12
Co-air (µg/m3)/-		/0.1-16.4	/0.9-16.0	/14.6-37.4
Co-EBC (ng/L)	/29.5-58.9/701-3198*		/2598-36989*/2197-43645*	
Co-U (µg/g C^)/0.03-0.21/0.88-2.76*/8.42-190.3*/3.74-25.6*				
W -air (µg/m3)/-		/<0.01	/0.01-0.2	/1.1-4.9
W -EBC (ng/L)	/<92.5	/<92.5	/92.5-907	/2812-14079
W -U (µg/g C^)/<0.1-2.5 /<0.1-1.6 /1.0-8.0 /5.3-26.4				
MDA-EBC (nM)	/7.0-8.5	/6.3-14.6	/12.4-16.6	/6.5-44.0°

C^: Creatinine
°: P < 0.05 versus control
*: P < 0.01 versus control

Reliability : (2) valid with restrictions
Low number of workers examined; impact of smoking behaviour on individual biomonitoring results not reported

Flag : Critical study for SIDS endpoint
14.03.2005 (80)

Type of experience : other: Biological Monitoring

Method : Workers from different workshops of a hard metal producing plant participated in personal air sampling and urine biomonitoring. Furthermore ambient air sampling was done at their workplaces.
- 87 workers (86 male and 1 female, median age of 42 years (range 22-58) and a mean duration of exposure of 13 years (range 1-27 years)) participated in the study
- 33 people not occupationally exposed to tungsten were participating as controls
- Stationary and personal air sampling over a mean period of 4 h
- Tungsten was analysed by inductively coupled plasma spectroscopy with mass spectrometry (ICP/MS)
- Iridium (193Ir) was used as an internal standard
- Calibration was performed with aqueous tungsten standard solutions
- The detection limit in urine was 0.05 µg/l

Remark : The authors of the study concluded that the bioavailability of tungsten increases in the order: tungsten metal, tungsten carbide, tungstenate. Significant methodological deficiencies in regard to the conclusion that tungsten carbide is bioavailable: It was not reported how the possibility was excluded that the tungsten carbide manufacturing area was contaminated by tungstenate e.g. from the nearby wet grinding workplaces. It is noted, that the provided data actually indicate that tungsten carbide may be less bioavailable than tungsten metal

Result : Maximum tungsten concentration was 417 µg/m³ in the production area for hard metals (cobalt 343 µg/m³ and nickel 30 µg/m³). The highest tungsten concentration in urine was 169 µg W/g creatinine and the mean value of 94 µg W/g creatinine. There was no correlation between the tungsten concentrations in air and urine. Highest tungsten concentration in urine (70.9 µg W/g creatinine) was found in a worker exposed to low concentrations of tungstenate (3.3 µg W/m3) (The highest urinary cobalt concentration was 228 µg Co/g creatinine and the mean was 28.5 µg Co/g creatinine. The highest urinary nickel concentration was 6.3 µg Ni/g

creatinine).

Ambient tungsten concentrations in different workshops (P=personal sampling; S=stationary sampling):

Workplace	Sample	n	µg W/m³
Forming	P	5	7.8-97.4
	S	1	6.2
Pressing	P	3	5.3-211.0
Powder process.	P	4	177.0-254.0
WC production	P	1	19.1
Sintering	P	1	12.1
	S	1	5.9
Grinding (wet)	P	1	3.3
Grinding (dry)	P	1	81.3
Alloy prod.	P	2	125.0-417.0
	S	3	50.0-163.0

Urinary tungsten concentrations in workers from different workshops:

Work	n	µg W/g*		µg W/g**
Forming	23	10.7	(6.7-14.6)	9.5 (0.33-33.1)
Press.	30	8.6	(4.1-13.1)	6.5 (1.5-71.0)
Alloy	3	24.9	(-34.9-84.8)	21.6 (2.6-50.5)
Powder	14	12.2	(8.0-16.5)	11.6 (2.6-25.1)
WC	4	42.1	(4.3-79.9)	48.9 (10.0-60.6)
Sinter.	6	12.5	(-5.7-30.7)	5.5 (2.1-46.8)
Grind.	5	94.4	(11.2-177.5)	70.9 (10.6-168.6)
Maint.	2	3.4	(-21.1-27.8)	3.4 (1.5-5.3)

*µg W/g creatinine (mean and 95 % confidence interval)
**µg W/g creatinine (median and range)

Ambient and biological monitoring of different tungsten species (*mean + range):
Powder processing (n=4): metallic W at 203.5* µg W/m³ air (177-254), biomonitoring* 13.8 µg W/g creatinine (2.6-21.1)
Forming, pressing, sintering (n=8): tungsten carbide at 53.5* µg W/m³ air (5.3-211), biomonitoring 9.5* µg W/g creatinine (2.2-33.1)
Grinding (dry) (n=1): Tungsten oxide,tungsten carbide at 81.3 µg W/m³ air, biomonitoring 10.6 µg W/g creatinine
WC production (n=1): Tungsten carbide, tungsten oxide, metallic tungsten at 19.1 µg W/m³ air, biomonitoring 59.6 µg W/g creatinine
Grinding (wet) (n=1): tungstenate 3.3 µg W/m³ air, biomonitoring 70.9 µg W/g creatinine

Test condition : - 87 workers (86 male and 1 female, median age of 42 years (range 22-58) and a mean duration of exposure of 13 years (range 1-27 years)) participated in the study
- 33 people not occupationally exposed to tungsten were participating as controls
- Stationary and personal air sampling over a mean period of 4 h
- Tungsten was analysed by inductively coupled plasma spectroscopy with mass spectrometry
- Iridium (193Ir) was used as an internal standard
- Calibration was performed with aqueous tungsten standard solutions
- The detection limit in urine was 0.05 µg/l

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint
03.06.2005 (81)

Type of experience : other: Exposure assessment

Method : Breathing zone air and general atmosphere samples were collected in the

wet tool grinding area of a hard metal tool maintenance facility without exhaust ventilation system. Sample filters were analysed for tungsten carbide (as tungsten).

Remark : The authors discribed several measures to diminish the airborne heavy metal concentrations, including the use of local exhaust ventilation

Result : The concentration of tungsten carbide (measured as tungsten) in breathing zone air samples (n = 25) ranged from < 0.2 to 12.8 mg/m3 with a mean of 5.16 mg/m3. The employee time-weighted average shift exposures ranged from 0.72 to 8.06 mg/m3 with a mean of 3.93 mg/m3.

Reliability : (1) valid without restriction

25.02.2005 (82)

Type of experience : other: Biological Monitoring

Method : From 4 patients with history of hard metal exposure and whose chest X-rays suggest stage II sarcoidosis specimens of open lung biopsy (n=3), BALF (n=3), blood, urine, pubic hair (n=3), nails (n=3) and sperm (n=1) were collected and analysed for tungsten levels.

Result : The workers also contained highly elevated tungsten levels in several biological materials (lung tissue, BALF, blood, urine, pubic hair, sperm, and nails). On the other hand, some biotic tungsten levels matched control values and no correlation between severity of disease and metal contents could be drawn from the data.

Ratios of tungsten found relative to control values

	Pat. 1	Pat. 2	Pat. 3	Pat. 4
Lung tissue	82307	5200	-	4320
BALF	40	20	20	-
Blood	-	2	1	-
	-	-	2*	-
	12**	-	-	-
Urine	30	1	7	2
	57*	-	8*	-
	32**	-	-	-
Pubic hair	-	3	142	-
	-	-	276*	-
Nails	-	24	1325	18
	-	-	1036*	-
Sperm	-	-	37	-
	-	-	655*	-

*) After 5 months
**) After 18 months
Pat.= Patient No.

Reliability : (2) valid with restrictions
No quantitative informations on exposure

14.03.2005 (83)

Type of experience : other: Biological Monitoring

Method : A patient with history of hard metal exposure for many years was examined 4 years after cessation of exposure. The chest X-rays and histological examination showed diffuse interstitial fibrosis and severe perivascular and peribronchiolar fibrosis. Specimens of open lung biopsy, BALF, blood and urine were collected and analysed for tungsten levels together with specimens from 17 control persons.

Remark : No quantitative informations on exposure. Tungsten accounted for 7.5 % of the total particulate matter at the workplace, iron for 10 %, and cobalt for 8 % (no information available on the rest of the particulate matter).

Result : Higher than control levels of tungsten were found in lung tissue, bronchoalveolar lavage fluid (BALF), blood, and urine:

Amounts and ratios relative to controls of tungsten found
(n= 17; mean values of 4 determinations)

	Worker (ng/g)	Control (ng/g)	Ratio
Lung tissue	107,000	1.5	71,330
BALF	60	1.5	40
Blood	1.35	0.4	3.4
Urine	12	0.7	17.1

Reliability : (2) valid with restrictions
Basic data given

14.03.2005 (84)

Type of experience : other: Patch testing of workers

Method : Patch testing with sodium tungstate was performed in 853 persons that are still or had been working in hard metal manufacture.

Result : There are no allergic reactions in patch testing of hard metal workers with sodium tungstate.

Reliability : (2) valid with restrictions
No quantitative informations on exposure, no informations about possible coexposure to cobalt

25.02.2005 (85)

Type of experience : other: Biological Monitoring

Method : From 251 patients with history of hard metal exposure (23 of them were diagnosed as diseased subjects affected by asthma and/or lung fibrosis) specimens of blood, urine, pubic hair and toe nails were collected and analysed for tungsten levels. Additionally tungsten concentration in workplace air was measured.

Result : Tungsten in airborne dust collected in the breathing zone of 4 factories in Italy (Bergamo province)

Factory	Operation	Metal Concentration (mg/m3) Fixed dust sampling	Personal monitor Total dust	Personal monitor < 7 µm	Personal monitor Total dust
A	weighing	32	2.1		150
A	grinding	62	2.4		77
B	weighing	20	3.1		70
C	grinding	10.2	0.75		53
C	grinding	2.1	0.13		22
D	weighing	0.14	0.023		0.73

Amounts of tungsten found in biological specimens of hard metal workers (Bergamo group)

	n	Metal content (mean +- SD) Exposed workers	Unexposed subjects
Blood	43	1.2 +- 1.6 µg/l	0.39 µg/l
Urine	78	6.7 +- 19.4 µg/l	0.32 µg/l
Pubic hair	75	2147 +- 5151 ng/g	12.4 ng/g
Toe nails	82	3056 +- 10760 ng/g	18.0 ng/g

Amounts of tungsten found in biological specimens of hard metal workers (Milan group)

/ n /Metal content (mean +- SD)
/ /Exposed workers
Blood /16 /1.29 +- 2.7 µg/l
Urine /21 /9.32 +- 6.5 µg/l
Pubic hair /20 /7018 +- 16570 ng/g
Toe nails /23 /17298 +- 32470 ng/g
BALF /24 /448 +- 602 µg/l*
*) 97.1 % in sediment, 2.9 % in supernatant

Amounts of tungsten found in air and in urine of hard metal workers (Pavia group)

/ n /Metal content (mean +- SD)
/ /Exposed workers
air /23 /0.026 +- 0.043 mg/m3
Urine /23 /2.29 +- 2.79 µg/l

Amounts of tungsten found in biological specimens of hard metal workers (Turin group)

/ n /Metal content (mean +- SD)
/ /Exposed workers
Urine /24 /12.8 +- 14.7 µg/l
Pubic hair /24 /9585 +- 9159 ng/g

Metal content in BALF of a diseased hard metal worker
Time of analysis after end of exposure/ tungsten (µg/l)
6 months / 689
8 months /1350
12 months / 700
18 months / 340

Reliability : (1) valid without restriction
14.03.2005 (86)

Type of experience : Human - Epidemiology

Method : A historical cohort was set up of all workers who had worked in a hard metal producing site for at least 3 months since its opening date in the late 1940s. A full job history could be obtained for 95 % of the subjects. The cohort was followed up from January 1968 to December 1992.

Result : Excess mortality from lung cancer was found among hard metal production workers which cannot be attributed to smoking alone. This excess occurred mostly in subjects exposed to unsintered hard metal dust (no informations on cobalt exposure given).

Reliability : (2) valid with restrictions
No quantitative informations on exposure, no informations about possible coexposure to cobalt
25.02.2005 (87)

Type of experience : other: Exposure assessment

Method : The dust collected at the workplaces and the dust of the lungs of workers with hard metal lung fibrosis (dust isolated using the formamide technique) were analysed qualitatively and quantitatively.

Result : Qualitative dust analysis showed that the metals tungsten, cobalt, and titanium were present.
The table shows the results of analysis of dusts at two different workplaces in the hard metal production (mixing dept. and conglomeration dept.) and of

dust from a worker's lung.

% metal content in dusts

Metal	/Mixing	/Conglomeration	/worker's lung dust
Tungsten	/67.80	/76.10	/63.80
Cobalt	/21.20	/ 7.60	/12.85
Titanium	/ 1.75	/ 0.00	/ 9.10
Iron oxide	/ 2.25	/ 0.30	/12.40
Sum	/93.00	/84.00	/98.15

Reliability : (1) valid without restriction
25.02.2005 (88)

Type of experience : other: Biological Monitoring

Method : Multielemental analysis using neutron activation was done on urine, whole blood, pubic hair and toenails of 30 workers occupationally exposed to hard metal dust.

Result : Tungsten concentration in hard metal dust exposed workers:

Group	/Tungsten concentration (ng/g wet weight) /Urine	/Blood	/Pubic hair	/Toenails
A (n=10)	/12	/3	/12000	/17000
B (n=7)	/44	/2.2	/ 3900	/ 2035
C (n=13)	/ 2	/0.8	/ 837	/ 1200
Contr. (n=3)	/ 0.4	/ 4.2	/ 15	/ 18

A,B,C: Different factories

Reliability : (1) valid without restriction
14.03.2005 (89)

Type of experience : Human - Epidemiology

Method : It was examined whether there is an elevated mortality from lung cancer, colon cancer or ishemic heart disease from 1970-1984 in 317 deceased workers of the General Electric Co. plant at Warren/Michigan, USA manufacturing products made of cemented tungsten carbide containing cobalt.

Remark : Workers were exposed to cobalt dust also.

Result : No significantly elevated risk of colon cancer was noted. The odds ratio for ischemic heart disease was higher in the group with longer employment and in those over 65 years old. There is some biological plausibility for an association of cardio-vascular disease and cobalt exposure. The pattern of elevated odds ratios for lung cancer was similar to that of cardiovascular diseases but due to the smaller number of cases these data are difficult to interpret.

Tumor incidences in deceased workers 1970-1984 (n=317)

Tumor type	/Obs.	/Exp.US/O:E	/Exp.GE/O:E
Large intestine	/8	/6.7 /1.20	/9.2 /0.87
Lung	/30	/25.5 /1.18	/27.2 /1.10
Isch.Heart Dis.	/149	/114.9 /1.30	/126.0 /1.18

Reliability : (2) valid with restrictions
No quantitative informations on exposure available.
25.02.2005 (90)

5.11 ADDITIONAL REMARKS

Type : Behaviour

Method : Hard metal dust containing 71.4 % tungsten, 24 % cobalt and 0.445 % tantalum was activated by neutron bombardment. 2 mg each of the washed solid material were resuspended in each 2 ml of human blood plasma, human lung tissue cytosol homogenate, 0.9 % NaCl, 10 mM phosphate buffer (pH 7.5), and distilled water. The probes were incubated at 25°C for 16 hrs. Afterwards the probes were centrifuged and duplicate samples of the supernatant (100 µl) were removed and analysed for radioactivity.

Result : The solubility of [187W]-tungsten from neutron-activated hard metal dust in lung cytosol, blood plasma, NaCl, phosphate buffer and water was very low (<= 1 % of total radioactivity).

Reliability : (1) valid without restriction

25.02.2005 (91)

Type : Behaviour

Method : 200 mg of tungsten carbide dust were dissolved in 100 ml of the following media:
Distilled water
0.3% hydrochloric acid
0.22% sodium bicarbonate solution
0.1 N lactic acid solution.
The solubility was determined after 1, 3, 30 and 90 days.

Result : Tungsten carbide is more soluble in an alkaline medium with a pH similar to that of certain areas of the body. In gastric juice it is only scarcely soluble. The solubility in the other media is given in the table.

Table: Solubility of tungsten carbide (in mg/l)

	Exposure Time (Days)			
Medium	/1	/3	/30	/90
Dist. Water	/ 75	/120	/180	/ 200
Na-bicarbonate	/160	/240	/500	/1400
Lactic acid	/ 70	/180	/200	/ 400

Reliability : (4) not assignable
No further study details reported. No information on purity of test substance

16.11.2005 (41)

Type : Biochemical or cellular interactions

Result : Tungsten carbide (1.5 mg/ml) did not stimulate the production of thiobarbituric acid-reactive substances from arachidonic acid (marker for arachidonic acid peroxidation) in isolated rat macrophages.

Reliability : (2) valid with restrictions

25.02.2005 (92)

Type : Biochemical or cellular interactions

Method : Deoxyribose degradation by tungsten carbide was measured in vitro in the presence of hydrogen peroxide and ascorbate.

Result : The deoxyribose degradation induced by tungsten carbide was relatively high when compared to other carbides. There was no direct relationship between deoxyribose degradation ability and cytotoxicity towards macrophages.

Reliability : (2) valid with restrictions

25.02.2005 (93)

Type : Biochemical or cellular interactions

Result : Tungsten carbide was a poor catalyst for the decomposition of hydrogen peroxide into oxygen and water. Aqueous buffered suspensions of tungsten carbide did not show any potential for free radical release.

Reliability : (2) valid with restrictions
25.02.2005 (94)

Type : Cytotoxicity

Method : Rat alveolar macrophages were treated in-vitro with maximum noncytotoxic doses (50 µg/ml) of tungsten carbide and production of inflammatory mediators (interleukin-1, tumor necrosis factor-alpha, fibronectin and cystatin-C) was measured.

Result : In-vitro treatment of rat alveolar macrophages did not affect the production of inflammatory mediators.

Reliability : (2) valid with restrictions
25.02.2005 (44)

Type : Cytotoxicity

Method : Mouse peritoneal macrophages and rat alveolar macrophages were treated with tungsten carbide up to 500 µg/1 000 000 cells.

Result : No effects on LDH release were observed. Morphological studies showed a swelling of cells which was interpreted as an intense phagocytosis process.

Reliability : (2) valid with restrictions
25.02.2005 (95)

Type : Cytotoxicity

Method : Mouse peritoneal macrophages and rat alveolar macrophages were treated with tungsten carbide up to 200 µg/1 000 000 cells.

Result : A dose-dependent increase of glucose-uptake was observed reflecting the intense metabolic activity. There were no changes in the activity of glucose-6-phosphate dehydrogenase and the superoxide anion release. Cell-associated plasminogen-activator activity was stimulated dose-dependently in mouse peritoneal macrophages.

Reliability : (2) valid with restrictions
25.02.2005 (96)

Type : Cytotoxicity

Method : Freshly isolated rat and human alveolar epithelial type II cells and alveolar macrophages were treated with tungsten carbide up to 1180 µg/100 000 cells.

Result : Tungsten carbide showed a low toxicity in rat cells and no toxicity in human cells up to the highest concentration tested (1180 µg/100 000 cells).

TD50 (in µg/100 000 cells) assessed by LDH release

rat alveolar type II cells	4468 (1354-14743*)
rat alveolar macrophages	591 (390-895*)

*) 95 % confidence interval

Reliability : (2) valid with restrictions
Non-GLP study but well conducted and reported

Flag : Critical study for SIDS endpoint
03.06.2005 (97)

Type : Cytotoxicity

Method : L2 rat lung epithelial cells were incubated for 24 hrs at 37°C with tungsten carbide dissolved in cell culture medium in concentrations of 5; 25 and 100 µg/ml. LDH as well as the reduction of pyruvate coupled with the oxidation of NADH was measured in the supernatant. After the incubation period the

cells were washed and stained for F-actin fibers.
Controls were incubated with physiological saline.

Result : Only minimal changes were observed in F-actin microfilaments of L2-cells after exposure to 5 and 25 µg/ml tungsten carbide; at 100 µg/ml tungsten carbide there was a noticeable disruption of the uniform distribution of L2-cell F-actin microfilaments. Tungsten carbide did not cause any change in cell viability (measured as LDH release and as trypan blue exclusion) compared to the control.

Reliability : (2) valid with restrictions
25.02.2005 (98)

Type : Cytotoxicity

Method : Isolated human lymphocytes were incubated with tungsten carbide (2 µg/ml).

Result : Tungsten carbide led to an early induction of apoptosis (15 min after start of incubation).

Reliability : (2) valid with restrictions
25.02.2005 (99)

Type : Cytotoxicity

Method : Isolated rat alveolar type II pneumocytes were incubated with 1175 µg/well tungsten carbide and the hexose monophosphate shunt activity of the cells was determined.

Result : Tungsten carbide did not influence the activity of the hexose monophosphate shunt.

Reliability : (2) valid with restrictions
25.02.2005 (100)

Type : Cytotoxicity

Method : Human peripheral blood mononucleated cells were incubated with 33.3 - 100.0 µg/ml tungsten carbide (purity 99.5 %; median particle diameter < 1 µm) and induction of apoptosis was measured
1) by measuring the externalisation of phosphatidyl serine
2) by flow cytometry
3) by cell death ELISA measuring histone-bound DNA fragments in the cytosol.

Result : Tungsten carbide induced apoptosis in human peripheral blood mononuclear cells (PBMC); the apoptotic activity was sensitive to the caspase-9 inhibitor. Apoptotic activity of tungsten carbide was confirmed by flow cytometry and by cell death ELISA. Tungsten carbide remained as particles in the incubation medium and was progressively phagocytosed by monocytes.

Reliability : (2) valid with restrictions
25.02.2005 (101)

Type : Distribution

Method : 10 ml of human whole blood or 5 ml of human lung homogenate (corresponding to ca. 1 g fresh lung tissue) were incubated separately for 20 min at 37°C with [187W]-sodium tungstate in concentrations of 0.1-48 ng tungsten/ml blood or 0.9-660 ng tungsten/g lung wet weight.
The blood was then centrifuged at 3000 rpm to separate the erythrocytes from blood plasma and the plasma was then subjected to gel filtration on Sephadex G 150 resin.

The lung homogenate was subjected to differential centrifugation for subcellular fractionation into nuclear fraction, mitochondrial fraction, lysosomal fraction, microsomal fraction and cytosol.

In another experiment 5 aliquots of 2.5 ml each of the [187W]-labelled lung cytosol were incubated with 2.5 ml of native fresh human blood plasma for 20 min at 37°C and then the mixture was subjected to gel filtration on Sephadex
G 150 resin.

Result : The subcellular distribution after incubation of lung tissue homogenate with [187W]-sodium tungstate is shown in the table.

Fraction /% radioactivity of total homogenate
lung homogenate /100.0
nuclear fraction / 4.3 +- 0.4
mitochondrial fract. / 1.7 +- 0.2
lysosomal fraction / 0.8 +- 0.1
microsomal fraction / 1.9 +- 0.4
cytosol / 91.3 +- 0.5

After incubation of whole blood with [187W]-sodium tungstate > 90 % of the radioactivity were found in the plasma and > 90 % thereof were found in the low molecular weight fraction after gel filtration of the plasma.
Gel filtration of the cytosol (without and with mixing with native fresh plasma) yielded an elution pattern similar to that of the plasma.

Reliability : (2) valid with restrictions
25.02.2005 (91)

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